



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

8 January 2018
EMA/PRAC/9221/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 08-11 January 2018

Chair: June Raine – Vice-Chair: Almath Spooner

08 January 2018, 13:00 – 19:30, room 3/A

09 January 2018, 08:30 – 19:30, room 3/A

10 January 2018, 08:30 – 19:30, room 3/A

11 January 2018, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

25 January 2018, 09:00-12:00, room 9/B, via teleconference

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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



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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held on 08-11 January 2018. See January 2018 PRAC minutes (to be published post February 2018 PRAC meeting).

1.2. Agenda of the meeting on 08-11 January 2018

Action: For adoption

1.3. Minutes of the previous meeting on 27-30 November 2017

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

2.3.1. Hydroxyethyl starch (HES)¹ (NAP) - EMEA/H/A-107i/1457

Applicants: Fresenius Kabi Deutschland GmbH (Volulyte, Voluven), B. Braun Melsungen AG (Tetraspan, Venofundin), Seruwerk Bernburg AG (Hesra); various

PRAC Rapporteur: Patrick Batty; PRAC Co-rapporteur: Ulla Wändel Liminga

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

Action: For adoption of a recommendation to CMDh

¹ Solution for infusion

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures²

None

3.5. Others

None

4. Signals assessment and prioritisation³

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Adalimumab – AMGEVITA (CAP), CYLTEZO (CAP), HUMIRA (CAP), IMRALDI (CAP), SOLYMBIC (CAP)

Applicant(s): AbbVie Limited (Humira), Amgen Europe B.V. (Amgevita, Solymbic), Boehringer Ingelheim International GmbH (Cyltezo), Samsung Bioepis UK Limited (Imraldi)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of lichenoid keratosis

Action: For adoption of PRAC recommendation

EPITT 19128 – New signal

Lead Member State(s): SE

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

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

4.1.2. Apixaban – ELIQUIS (CAP)

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

PRAC Rapporteur: Menno van der Elst

Scope: Signal of tubulointerstitial nephritis

Action: For adoption of PRAC recommendation

EPITT 19127 – New signal

Lead Member State(s): NL

4.1.3. Apixaban – ELIQUIS (CAP); edoxaban – LIXIANA (CAP), ROTEAS (CAP); Serotonin and noradrenaline reuptake inhibitors (SNRI): desvenlafaxine (NAP); duloxetine - ARICLAIM (CAP), CYMBALTA (CAP), DULOXETINE LILLY (CAP), DULOXETINE MYLAN (CAP), DULOXETINE ZENTIVA (CAP), XERISTAR (CAP), YENTREVE (CAP); milnacipran (NAP); venlafaxine (NAP) Selective serotonin reuptake inhibitors (SSRI): citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); fluvoxamine (NAP); paroxetine (NAP); sertraline (NAP)

Applicant(s): Bristol-Myers Squibb / Pfizer EEIG (Eliquis), Daiichi Sankyo Europe GmbH (Lixiana, Roteas), Eli Lilly Nederland B.V. (Ariclaim, Cymbalta, Duloxetine Lilly, Xeristar, Yentreve), Generics UK Limited (Duloxetine Mylan); Zentiva k.s. (Duloxetine Zentiva); various

PRAC Rapporteur: To be appointed

Scope: Signal of drug interaction between apixaban or edoxaban and SSRI and/or SNRI leading to increased risk of bleeding

Action: For adoption of PRAC recommendation

EPITT 19139 – New signal

Lead Member State(s): ES, NL, UK

4.1.4. Concentrate of proteolytic enzymes enriched in bromelain – NEXOBRID (CAP)

Applicant(s): MediWound Germany GmbH

PRAC Rapporteur: Valerie Strassmann

Scope: Signal of haemorrhage

Action: For adoption of PRAC recommendation

EPITT 19133 – New signal

Lead Member State(s): DE

4.1.5. Lenalidomide – REVLIMID (CAP)

Applicant(s): Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

Action: For adoption of PRAC recommendation

EPITT 19130 – New signal

Lead Member State(s): FR

4.1.6. Pembrolizumab – KEYTRUDA (CAP)

Applicant(s): Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Signal of aseptic meningitis

Action: For adoption of PRAC recommendation

EPITT 19115 – New signal

Lead Member State(s): NL

4.2. New signals detected from other sources

4.2.1. Adalimumab – AMGEVITA (CAP), CYLTEZO (CAP), HUMIRA (CAP), IMRALDI (CAP), SOLYMBIC (CAP); infliximab – FLIXABI (CAP), INFLECTRA (CAP), REMICADE (CAP), REMSIMA (CAP)

Applicant(s): AbbVie Limited (Humira), Amgen Europe B.V. (Amgevita, Solymbic), Boehringer Ingelheim International GmbH (Cyltezo), Celltrion Healthcare Hungary Kft. (Remsima), Hospira UK Limited (Inflectra), Janssen Biologics B.V. (Remicade), Samsung Bioepis UK Limited (Flixabi, Imraldi)

PRAC Rapporteur: To be appointed

Scope: Signal of risk of lymphoma in patients with inflammatory bowel disease

Action: For adoption of PRAC recommendation

EPITT 19121 – New signal

Lead Member State(s): DE, FI, SE, UK

4.2.2. Hormonal contraceptives:

Chlormadinone, estradiol (NAP); chlormadinone acetate, ethinylestradiol (NAP); conjugated estrogens, medrogestone (NAP); conjugated estrogens, medroxyprogesterone acetate (NAP); conjugated estrogens, norgestrel (NAP); cyproterone, ethinylestradiol (NAP); cyproterone acetate, estradiol valerate (NAP); desogestrel (NAP); desogestrel, ethinylestradiol (NAP); dienogest, estradiol⁴ (NAP); dienogest, ethinylestradiol (NAP); drospirenone, estradiol (NAP); drospirenone, ethinylestradiol (NAP); estradiol, estriol, levonorgestrel (NAP); estradiol, gestodene (NAP); estradiol, levonorgestrel (NAP); estradiol, medroxyprogesterone acetate (NAP); estradiol, nomegestrol acetate (NAP); estradiol, norethisterone (NAP); estradiol, norgestimate (NAP); estradiol (17-beta), progesterone (NAP); estradiol (17-beta), trimegestone (NAP); estradiol valerate, norgestrel (NAP); ethinylestradiol, etonogestrel (NAP); ethinylestradiol, etynodiol (NAP);

⁴ Contraception indication

ethinylestradiol, gestodene⁵ (NAP); ethinylestradiol, gestodene⁶ (NAP); ethinylestradiol, levonorgestrel (NAP); ethinylestradiol, lynestrenol (NAP); ethinylestradiol, norethisterone (NAP); ethinylestradiol, norgestimate (NAP); ethinylestradiol, norgestrel (NAP); levonorgestrel, ethinylestradiol; ethinylestradiol⁷ (NAP); levonorgestrel (NAP); medroxyprogesterone (NAP); mestranol, norethisterone (NAP); nomegestrol (NAP); nomegestrol acetate, estradiol – ZOELY (CAP); norelgestromin, ethinyl estradiol – EVRA (CAP), NAP; norethisterone (NAP)

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

PRAC Rapporteur: To be appointed

Scope: Signal of a known association between hormonal contraceptives and breast cancer following a recent publication

Action: For adoption of PRAC recommendation

EPITT 19143 – New signal

Lead Member State(s): DE, DK, FI, FR, NL, PL, SE, UK

4.2.3. Hormonal contraceptives:

Chlormadinone, estradiol (NAP); chlormadinone acetate, ethinylestradiol (NAP); conjugated estrogens, medrogestone (NAP); conjugated estrogens, norgestrel (NAP); cyproterone, ethinylestradiol (NAP); cyproterone acetate, estradiol valerate (NAP); desogestrel (NAP); desogestrel, ethinylestradiol (NAP); dienogest, estradiol⁸ (NAP); dienogest, ethinylestradiol (NAP); drospirenone, estradiol (NAP); drospirenone, ethinylestradiol (NAP); estradiol, estriol, levonorgestrel (NAP); estradiol, gestodene (NAP); estradiol, levonorgestrel (NAP); estradiol, medroxyprogesterone acetate (NAP); estradiol, nomegestrol acetate (NAP); estradiol, norethisterone (NAP); estradiol, norgestimate (NAP); estradiol (17-beta), progesterone (NAP); estradiol (17-beta), trimegestone (NAP); estradiol valerate, norgestrel (NAP); ethinylestradiol⁹ (NAP); ethinylestradiol, conjugated estrogens, medroxyprogesterone acetate (NAP); ethinylestradiol, etonogestrel (NAP); ethinylestradiol, etynodiol (NAP); ethinylestradiol, gestodene¹⁰ (NAP); ethinylestradiol, gestodene¹¹ (NAP); ethinylestradiol, levonorgestrel (NAP); ethinylestradiol, norethisterone (NAP); ethinylestradiol, norgestimate (NAP); ethinylestradiol, norgestrel (NAP); levonorgestrel (NAP); levonorgestrel, ethinylestradiol; lynestrenol (NAP); medroxyprogesterone (NAP); mestranol, norethisterone (NAP); nomegestrol (NAP); nomegestrol acetate, estradiol – ZOELY (CAP); norelgestromin, ethinyl estradiol – EVRA (CAP), NAP; norethisterone (NAP)

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

PRAC Rapporteur: To be appointed

Scope: Signal of suicidality with hormonal contraceptives following a recent publication

Action: For adoption of PRAC recommendation

EPITT 19144 – New signal

Lead Member State(s): DE, DK, FI, FR, NL, PL, SE, UK

⁵ All route of administrations except transdermal

⁶ Transdermal application

⁷ Combination pack

⁸ Contraception indication

⁹ Combination pack

¹⁰ All route of administrations except transdermal

¹¹ Transdermal application

4.2.4. Hydrochlorothiazide (NAP);
Aliskiren, hydrochlorothiazide – RASILEZ HCT (CAP); amlodipine, valsartan, hydrochlorothiazide – COPALIA HCT (CAP); amlodipine besylate, valsartan, hydrochlorothiazide – DAFIRO HCT (CAP), EXFORGE HCT (CAP); irbesartan, hydrochlorothiazide – COAPROVEL (CAP), IFIRMACOMBI (CAP), IRBESARTAN HYDROCHLOROTHIAZIDE ZENTIVA (CAP), IRBESARTAN/HYDROCHLOROTHIAZIDE TEVA (CAP), KARVEZIDE (CAP); telmisartan, hydrochlorothiazide - ACTELSAR HCT (CAP), KINZALKOMB (CAP), MICARDISPLUS (CAP), PRITORPLUS (CAP), TOLUCOMBI (CAP)

Applicant(s): Actavis Group PTC ehf (Actelsar HCT), Bayer Pharma AG (Kinzalkomb, PritorPlus), Boehringer Ingelheim International (MicardisPlus), Krka, d.d. (Ifirmacombi, Tolucombi), Noden Pharma DAC (Rasilez HCT), Novartis Europharm Limited (Copalia HCT, Dafiro HCT), Sanofi-aventis groupe (Irbesartan Hydrochlorothiazide Zentiva, Karvezide), Sanofi Clir SNC (CoAprovel), Teva B.V. (Irbesartan/Hydrochlorothiazide Teva); various

PRAC Rapporteur: To be appointed

Scope: Signal of skin cancer

Action: For adoption of PRAC recommendation

EPITT 19138 – New signal

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

4.3. Signals follow-up and prioritisation

4.3.1. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/SDA/009

Applicant(s): Eli Lilly Nederland B.V

PRAC Rapporteur: Carmela Macchiarulo

Scope: Signal of gastrointestinal stenosis and obstruction

Action: For adoption of PRAC recommendation

EPITT 18931 – Follow-up to September 2017

4.3.2. Megestrol (NAP); Vitamin K antagonists: acenocoumarol (NAP); fluindione (NAP); phenindione (NAP); phenprocoumon (NAP); warfarin (NAP)

Applicant(s): various

PRAC Rapporteur: Almath Spooner

Scope: Signal of drug interaction leading to elevated international normalised ratio (INR)/haemorrhage with megestrol and vitamin K antagonists

Action: For adoption of PRAC recommendation

EPITT 18910 – Follow up to September 2017

4.3.3. Methotrexate - JYLAMVO (CAP), NORDIMET (CAP) - EMEA/H/C/003983/SDA/002.1; NAP

Applicant(s): Nordic Group B.V. (Nordimet); Therakind Limited (Jylamvo); various

PRAC Rapporteur: Martin Huber

Scope: Signal of pulmonary alveolar haemorrhage

Action: For adoption of PRAC recommendation

EPITT 18850 – Follow-up to September 2017

4.3.4. Pemetrexed - ALIMTA (CAP) - EMEA/H/C/000564/SDA/027

Applicant(s): Eli Lilly Nederland B.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Signal of nephrogenic diabetes insipidus

Action: For adoption of PRAC recommendation

EPITT 18930 – Follow-up to September 2017

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Caplacizumab - EMEA/H/C/004426, Orphan

Applicant: Ablynx NV

Scope: Treatment of acquired thrombotic thrombocytopenic purpura (aTTP)

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

5.1.2. Dolutegravir, rilpivirine - EMEA/H/C/004427

Scope: Treatment of human immunodeficiency virus-1 (HIV-1) infection in virologically-suppressed (HIV-1 RNA¹²<50 c/mL) adult subjects without known or suspected resistant to either components

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

5.1.3. Pemetrexed - EMEA/H/C/003958

Scope: Treatment of malignant pleural mesothelioma and non-small cell lung cancer (NSCLC)

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

¹² Ribonucleic acid

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

5.2.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/II/0018, Orphan

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Updated RMP (version 8.0) to address the requests made in the conclusion of procedure IB/14, including updates from pre-approval information to post-marketing information, an update of the number of patients treated in clinical trials, special access schemes and commercial distribution, change in the development of the custom-made device, postponement of pharmacokinetic (PK) study CUV052 (study on the PK profile in erythropoietic protoporphyria (EPP) patients after administration of implant 1 on day 1 and implant 2 on day 60), update on timelines for safety extension study CUV037 from Q12013 to Q12018, update on timelines for on-going and planned pharmacovigilance studies, key elements of educational and training programme, replacement of 'pigmentary lesions' by 'pigmentary expressions' and general update of safety information

Action: For adoption of PRAC Assessment Report

5.2.2. Cetrorelix - CETROTIDE (CAP) - EMEA/H/C/000233/II/0064

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Updated RMP (version 5.0) in order to update the list of important identified risks by adding 'ovarian hyperstimulation syndrome' (OHSS) and removing injection site reactions (ISR). In addition, further minor RMP updates were introduced

Action: For adoption of PRAC Assessment Report

5.2.3. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/WS1342; ombitasvir, paritaprevir, ritonavir – VIEKIRAX (CAP) – EMEA/H/C/003839/WS1342

Applicant: AbbVie Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Updated RMP (version 4) to incorporate changes requested by PRAC (in procedures PSUSA/00010363/201701 and PSUSA/00010367/201701): addition of a new potential risk of depression and suicide as newly identified safety concerns; removal of off-label use and medication error as potential risks; renaming of the potential risk of development of resistance to lack of efficacy/risk of development of resistance. In addition, the commitment dates for 4 ongoing studies (on-going and planned additional pharmacovigilance studies/activities in the pharmacovigilance plan) have been revised

Action: For adoption of PRAC Assessment Report

5.2.4. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/WS1293/0115, PROMETAX (CAP) - EMEA/H/C/000255/WS1293/0115

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Updated RMP (version 9.0) to: 1) reflect milestone changes for study ENA713D2409: a drug utilisation study (DUS) on the appropriate use and estimate amount/type of inappropriate drug use of all doses of Exelon/Prometax patch, based on the PRAC outcome of procedures MEA 034.2 and MEA 035.1 protocol amendment version 2; 2)- remove the important identified risk 'pancreatitis' based on the PRAC outcome of procedure PSUSA/00002654/201501 finalised in September 2015; 3) discontinue the use of the targeted checklist to document cases of medication error/misuse based on the PRAC outcome of procedure PSUSA/00002654/201601 finalised in September 2016; 4) change the frequency of 'the effectiveness of risk minimisation measures for multiple patch use' from 6 monthly to annually based on the PRAC outcome of the fourth 6 monthly report. The RMP is also updated to include information on the submission of an interim analysis report for drug utilisation study (DUS) ENA713D2409 regarding the distribution of a healthcare professional (HCPs) letter in Japan, information on the request from the Brazilian health authority to include a statement in local Exelon patch leaflet to minimize the potential risk of skin irritation, information that the core data sheet (CDS) was amended to include 'nightmares' as an adverse drug reaction (ADR)

Action: For adoption of PRAC Assessment Report

5.2.5. Telbivudine - SEBIVO (CAP) - EMEA/H/C/000713/II/0048

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Caroline Laborde

Scope: Updated RMP (version 11.0) in order to reclassify the risk of lactic acidosis from an important potential risk to an important identified risk and to include a targeted questionnaire for fatal cases as additional risk minimisation measure as requested by the PRAC as part of the assessment of PSUSA/00002880/201608 adopted in April 2017

Action: For adoption of PRAC Assessment Report

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

5.3.1. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/II/0050

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to update the posology, method of administration and efficacy and safety information based on final results from study B0661025/CV185267: a phase IV trial to assess the effectiveness of apixaban compared with usual care anticoagulation in subjects with non-valvular atrial fibrillation (NVAf) undergoing cardioversion (EMANATE) listed as a post-authorisation efficacy study (PAES) in the RMP. The Package Leaflet and the RMP (version 19) are updated accordingly. In

addition, the MAH took the opportunity to update the list of addresses in the product information

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

5.3.2. [Bortezomib - BORTEZOMIB ACCORD \(CAP\) - EMEA/H/C/003984/X/0008](#)

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Line extension application to add a new strength of powder for solution for injection (1 mg) to the currently approved strength (3.5 mg) of Bortezomib Accord. The RMP (version 6.0) is updated accordingly

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

5.3.3. [Brentuximab vedotin - ADCETRIS \(CAP\) - EMEA/H/C/002455/II/0049, Orphan](#)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data from study C25002: a phase 1/2, non-randomised single arm study of brentuximab vedotin (SGN-35) in paediatric patients with relapsed or refractory systemic anaplastic large cell lymphoma or Hodgkin lymphoma (listed in the agreed paediatric investigation plan (PIP) covering the conditions of Hodgkin lymphoma and anaplastic large cell lymphoma for Adcetris (EMA-000980-PIP01-10-M04)). The RMP (version 11.0) is updated accordingly

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

5.3.4. [Canagliflozin - INVOKANA \(CAP\) - EMEA/H/C/002649/II/0034](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: Update of sections 4.1, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on cardiovascular events following the final results from CANVAS programme consisting of study DIA3008: a phase 3 randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus (T2DM); and study DIA4004: a phase 4 randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on renal endpoints in adult subjects with T2DM. The package leaflet and the RMP (version 7.2) are updated accordingly

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

5.3.5. [Canagliflozin, metformin - VOKANAMET \(CAP\) - EMEA/H/C/002656/II/0034](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.1, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on cardiovascular events following the final results from CANVAS programme consisting of study DIA3008: a phase 3 randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus (T2DM); and study DIA4004: a phase 4 randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on renal endpoints in adult subjects with T2DM. The package leaflet and the RMP (version 7.2) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to bring the product information in line with the latest QRD template (version 10)

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

5.3.6. [Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA \(CAP\) - EMEA/H/C/004391/II/0002/G](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Grouped variations to 1) submit the results of study GS-US-311-1089: a phase 3, randomized, double-blind, switch study to evaluate emtricitabine/tenofovir alafenamide (F/TAF) in human immunodeficiency virus 1 (HIV-1) positive subjects who are virologically suppressed on regimens containing emtricitabine/tenofovir disoproxil fumarate (FTC/TDF). The RMP (version 5.0) is updated accordingly; 2) update of the RMP to remove pancreatitis, convulsion, and cardiac conduction abnormalities as risks in the RMP in alignment with the RMP for Prezista (darunavir) and Rezolsta (darunavir/cobicistat)

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

5.3.7. [Diphtheria, tetanus, pertussis \(acellular, component\), hepatitis B \(rDNA\), poliomyelitis \(inactivated\) and haemophilus type B conjugate vaccine \(adsorbed\) - VAXELIS \(CAP\) - EMEA/H/C/003982/II/0021](#)

Applicant: MCM Vaccine B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 5.1 of the SmPC in order to update the efficacy section on immune persistence based on the final results from study PRI03C: a study on long-term persistence of hepatitis B and pertussis antibody responses in healthy 4 to 5 year old children previously vaccinated with a 2 dose or 3 dose infants series and toddler dose of Vaxelis or Infanrix Hexa (diphtheria, tetanus, pertussis (acellular, component) (Pa), hepatitis B (rDNA), poliomyelitis (inactivated) and haemophilus influenzae type-b conjugate vaccine (adsorbed)) listed as a P46 study in the paediatric investigation plan (PIP). The RMP (version 2.2) is updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes in Annex IIIa

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

5.3.8. [Exenatide - BYDUREON \(CAP\) - EMEA/H/C/002020/X/0048/G](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form (prolonged-release suspension for injection); 2) variation to align the product information for the approved Bydureon formulations (powder and solvent for prolonged-release suspension for injection, powder and solvent for prolonged-release suspension for injection in pre-filled pen) with the product information proposed for the new pharmaceutical form (prolonged-release suspension for injection in autoinjector). In addition, the MAH took the opportunity to introduce minor editorial changes in the SmPC. The RMP (version 28) is updated accordingly

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

5.3.9. [Febuxostat - ADENURIC \(CAP\) - EMEA/H/C/000777/II/0047](#)

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to reflect the results of preclinical study MRPO-2015-PKM-005: 'a pharmacokinetic study of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the concomitant oral administration of febuxostat or allopurinol' and clinical study REP-POPPK-MRP-2015-PKM-005: 'a population pharmacokinetic analysis from study titled pharmacokinetics of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the concomitant oral administration of febuxostat or allopurinol', investigating the drug-drug interaction with azathioprine when co-administered with febuxostat. The RMP (version 6.0) is updated accordingly. In addition, the MAH took the opportunity to correct typing errors and to bring the product information in line with the latest ORD template (version 10)

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

5.3.10. [Fosaprepitant - IVEMEND \(CAP\) - EMEA/H/C/000743/II/0037](#)

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include adolescents, infants, toddlers and children aged 6 months and older for prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 5.0) are updated accordingly

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

5.3.11. [Glecaprevir, pibrentasvir - MAVIRET \(CAP\) - EMEA/H/C/004430/II/0004](#)

Applicant: AbbVie Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to update

information on the use of Maviret in liver or kidney transplant patients, based on new clinical data from study M13-596 (MAGELLAN-2): a post-authorisation phase 3 study listed as a category 3 study in the RMP, which evaluated the efficacy and safety of the glecaprevir/pibrentasvir regimen in adult subjects with chronic hepatitis C virus genotypes 1-6 infection, who have received a liver or renal transplant. The package leaflet and the RMP (version 3.0) are updated accordingly

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

5.3.12. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/II/0008, Orphan

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of section 4.5 of the SmPC to include that CYP3A4¹³ substrates known to have a narrow therapeutic index should be administered with caution in patients receiving idebenone, based on the final study report for study SNT-I-017: an open-label study to assess the potential for pre-systemic inhibition of cytochrome P450 3A4 (CYP3A) by idebenone in healthy male subjects using midazolam as a substrate'. The package leaflet and the RMP (version 1.5) are updated accordingly. The provision of the study report fulfils MEA 005.1

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

5.3.13. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/II/0038

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Patrick Batty

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to reflect information from a recent cumulative safety review of cases of organising pneumonia. The Package Leaflet and Labelling are updated accordingly. The RMP (version 2.6) is also updated to extend the deadlines for submission of final clinical study report (CSR) for three studies linked to Annex II conditions

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

5.3.14. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0209

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 of the SmPC to amend the current warning on colon cancer and dysplasia based on the final report of the OPUS registry (P04808): a prospective, observational, non-interventional, post-marketing safety surveillance program in subjects with ulcerative colitis (UC). The provision of the study report fulfils MEA 121. In addition, the MAH took the opportunity to add a warning on screening tests for tuberculosis to align it with current medical practice, to add a reminder on the patient alert card in the package leaflet. Furthermore, the MAH introduced some editorial changes in line with the latest QRD

¹³ Cytochrome P450 3A4

template. The RMP (version 14.1) is updated accordingly

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

5.3.15. [Insulin aspart - FIASP \(CAP\) - EMEA/H/C/004046/II/0003/G](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Julie Williams

Scope: Grouped variations to: 1) update the RMP (version 2.0) to reclassify the risk of mix-up between basal and bolus insulin from a potential to an important identified risk; 2) update the secondary packaging material (carton, label, instructions for use (IFU)) design and change colour of selected plastic components from yellow to red. In addition, the MAH submitted as part of this variation a proposal for communication to healthcare professionals (HCPs) and patients (indirectly) regarding similarity between Fiasp and Tresiba (insulin degludec)

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

5.3.16. [Ivabradine - CORLENTOR \(CAP\) - EMEA/H/C/000598/WS1180, IVABRADINE ANPHARM \(CAP\) – EMEA/H/C/004187/WS1180, PROCORALAN \(CAP\) – EMEA/H/C/000597/WS1180](#)

Applicant(s): Les Laboratoires Servier (Corlentor, Procoralan), Anpharm Przedsiębiorstwo (Ivabradine Anpharm)

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.8 of the SmPC to add new adverse drug reactions (ADRs): ventricular tachycardia, ventricular fibrillation and Torsade de Pointes. The Package Leaflet and the RMP (version 6) are updated accordingly. In addition the MAH took the opportunity to align the product information with the latest QRD template (version 10)

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

5.3.17. [Lapatinib - TYVERB \(CAP\) - EMEA/H/C/000795/II/0050/G](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) submission of the final report for non-clinical study 09DMR047 (listed as a category 3 study in the RMP): a non-clinical mechanistic study related to lapatinib metabolite identification in dog plasma, bile and liver. The RMP (version 33) is updated accordingly; 2) change to the final due date of study EGF117165: an open-label, phase 2 study to evaluate biomarkers associated with response to subsequent therapies in subjects with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer receiving treatment with trastuzumab in combination with lapatinib or chemotherapy (category 1 study, ANX034.2) from June 2018 to June 2019 in the RMP and Annex II. In addition, the MAH took the opportunity to update the RMP to include the removal of two identified risks (rash, diarrhoea) and update missing information (hepatic impairment and renal impairment) in line with the recent PSUSA PRAC recommendation

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

5.3.18. Levetiracetam - KEPRA (CAP) - EMEA/H/C/000277/II/0169/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Grouped variations consisting of: 1) update of section 4.8 of the SmPC to add the adverse drug reaction (ADR) 'gait disturbance' to address the CHMP recommendation from P46/085; 2) update of section 4.2 of the SmPC to add dysgeusia as a potential experience post administration and update of section 4.5 of the SmPC to remove drug interaction with methotrexate in accordance with the latest levetiracetam company core data sheet; 3) update of section 4.6 to add information on 'women of childbearing potential' and to update the pregnancy section to address the PRAC recommendation from LEG 084.1. The package leaflet and the RMP (version 8) are updated accordingly

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

5.3.19. Moroctocog alfa - REFACTO AF (CAP) - EMEA/H/C/000232/II/0143

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update the existing safety, efficacy and pharmacokinetic information based on the final results from 1) study B1831005 (listed as a category 3 study in the RMP (MEA 111)): a non-randomized, open label study to evaluate the safety, efficacy, and pharmacokinetics (PK) of ReFacto AF in previously treated children less than 12 years of age with severe haemophilia A (factor VIII (FVIII):C<1%), already submitted in P46-143; 2) study B1831006 (listed as a category 3 study in the RMP (MEA 113)): an open-label study on the safety and efficacy of ReFacto AF in previously untreated patients (PUPs) in usual care settings, already submitted in P46-145). The RMP (version 12.0) is updated accordingly and include an update relating to study B1831083 (listed as a category 3 study in the RMP): an open-label, single-arm, post-authorisation pragmatic clinical trial on the safety and efficacy of moroctocog alfa in subjects with haemophilia A in usual care settings in China, already submitted as P46-144. Furthermore, the product information is brought in line with the latest QRD template (version 10) and amended to introduce an editorial change to the Czech local representative address in the package leaflet

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

5.3.20. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/II/0018/G, Orphan

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Grouped variations consisting of: 1) update of section 4.4 in order to remove the current warning on co-administration with pirfenidone and update of section 5.1 to include the results of study 1199.222: a phase IV, 12 week, open label, randomised, parallel group study to evaluate the safety, tolerability and pharmacokinetic (PK) of oral nintedanib in combination with oral pirfenidone in comparison with nintedanib alone in patients with idiopathic pulmonary fibrosis (IPF); 2) update of section 5.2 of the SmPC in order to include the results of study 1199.229 (listed as a category 3 study in the RMP): a phase 4, open

label, multidose, 2 groups study to investigate the drug-drug interaction (DDI) between nintedanib and pirfenidone in patients with IPF. The RMP (version 5.0) is updated accordingly. In addition, the MAH took the opportunity to implement some corrections to the French and Swedish translations

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

5.3.21. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0041

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include adjuvant treatment of adults and adolescents of 12 years of age and older with completely resected stage III and IV melanoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add efficacy and safety information from pivotal study CA209238: a phase 3, randomized, double-blind study of adjuvant immunotherapy with nivolumab versus ipilimumab after complete resection of stage IIIb/c or stage IV melanoma in subjects who are at high risk for recurrence. The package leaflet and the RMP (version 12.0) are updated accordingly. The MAH also took the opportunity to revise the due dates for two category 4 studies, namely study CA209172: a single-arm, open-label, multicentre clinical trial with nivolumab for subjects with histologically confirmed stage III (unresectable) or stage IV melanoma progressing post prior treatment containing an anti-CTLA4 monoclonal antibody; and study CA209171: an open-label, multicentre clinical trial with nivolumab monotherapy in subjects with advanced or metastatic squamous cell (Sq) non-small cell lung cancer (NSCLC) who have received at least one prior systemic regimen for the treatment of stage IIIb/IV SqNSCLC. In addition, the MAH took the opportunity to make minor editorial changes to the product information

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

5.3.22. Pomalidomide - IMNOVID (CAP) - EMEA/H/C/002682/II/0027, Orphan

Applicant: Celgene Europe Limited

PRAC Rapporteur: Patrick Batty

Scope: Update of sections 4.2, 4.4, and 4.8 of the SmPC in order to add new adverse drug reactions (ADR): Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) following a review of reports on severe skin reactions. 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

5.3.23. Sirolimus - RAPAMUNE (CAP) - EMEA/H/C/000273/II/0164

Applicant: Pfizer Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of patients with lymphangioleiomyomatosis. As a consequence, section 4.1, 4.2, 4.8, 5.1 and 5.2 of the

SmPC are updated. The package leaflet and the RMP (version 6.0) are updated accordingly. In addition, the MAH took the opportunity to make very minor formatting changes in the Labelling

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

5.3.24. [Sonidegib - ODOMZO \(CAP\) - EMEA/H/C/002839/II/0016](#)

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Update of Annex II to delete the condition 'post-authorisation efficacy study (PAES): submission of the final clinical study report (CSR) for study CLDE225A2201: a phase 2, randomized double-blind study of efficacy and safety of two dose levels of LDE225 (sonidegib) in patients with locally advanced or metastatic basal cell carcinoma, including an updated analysis of outcomes by aggressive vs. non-aggressive histological subtypes.' The RMP (version 7.0) is updated accordingly

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

5.3.25. [Tocilizumab - ROACTEMRA \(CAP\) - EMEA/H/C/000955/II/0074/G](#)

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped quality variations

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

6. Periodic safety update reports (PSURs)

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

6.1.1. [Afamelanotide - SCENESSE \(CAP\) - PSUSA/00010314/201706](#)

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. [Alectinib - ALECENSA \(CAP\) - PSUSA/00010581/201707](#)

Applicant: Roche Registration Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Ambrisentan - VOLIBRIS (CAP) - PSUSA/00000129/201706

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/201707

Applicant: Alexion Europe SAS

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Autologous CD34⁺ enriched cell fraction that contains CD34⁺ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) complementary deoxyribonucleic acid (cDNA) sequence - STRIMVELIS (CAP) - PSUSA/00010505/201705

Applicant: GlaxoSmithKline Trading Services Limited, ATMP¹⁴

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.6. Avanafil - SPEDRA (CAP) - PSUSA/00010066/201706

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Blinatumomab - BLINCYTO (CAP) - PSUSA/00010460/201706

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁴ Advanced therapy medicinal product

6.1.8. Brinzolamide, brimonidine tartrate - SIMBRINZA (CAP) - PSUSA/00010273/201706

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Bromfenac - YELLOX (CAP) - PSUSA/00000436/201705

Applicant: PharmaSwiss Ceska Republika s.r.o

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Canakinumab - ILARIS (CAP) - PSUSA/00000526/201706

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Chlorhexidine - UMBIPRO (Art 58¹⁵) - EMEA/H/W/003799/PSUV/0003

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.12. Daclatasvir - DAKLINZA (CAP) - PSUSA/00010295/201707

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Daclizumab - ZINBRYTA (CAP) - PSUSA/00010518/201705

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia

¹⁵ 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)

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Dasatinib - SPRYCEL (CAP) - PSUSA/00000935/201706

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Edotreotide - SOMAKIT TOC (CAP) - PSUSA/00010552/201706

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Efmoroctocog alfa - ELOCTA (CAP) - PSUSA/00010451/201706 (with RMP)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Elotuzumab - EMLICITI (CAP) - PSUSA/00010500/201705

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Emedastine - EMADINE (CAP) - PSUSA/00001207/201705

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Fidaxomicin - DIFICLIR (CAP) - PSUSA/00001390/201705

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Qun-Ying Yue
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.20. [Follitropin delta - REKOVELLE \(CAP\) - PSUSA/00010554/201705](#)

Applicant: Ferring Pharmaceuticals A/S
PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.21. [Galsulfase - NAGLAZYME \(CAP\) - PSUSA/00001515/201705](#)

Applicant: BioMarin Europe Ltd
PRAC Rapporteur: Patrick Batty
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.22. [Glycerol phenylbutyrate - RAVICTI \(CAP\) - PSUSA/00010454/201705](#)

Applicant: Horizon Pharma Ireland Limited
PRAC Rapporteur: Carmela Macchiarulo
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.23. [Human fibrinogen, human thrombin - EVARREST \(CAP\), EVICEL \(CAP\), RAPLIXA \(CAP\), TACHOSIL \(CAP\) - PSUSA/00010297/201706](#)

Applicants: Mallinckrodt Pharmaceuticals Ireland Limited (Raplixia), Omrix Biopharmaceuticals N. V. (Evarrest, Evicel), Takeda Austria GmbH (TachoSil)
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.24. [Human papillomavirus \[types 6, 11, 16, 18, 31, 33, 45, 52, 58\] \(recombinant, adsorbed\) - GARDASIL 9 \(CAP\) - PSUSA/00010389/201706](#)

Applicant: MSD Vaccins
PRAC Rapporteur: Julie Williams
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.25. Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - GARDASIL (CAP), SILGARD (CAP) - PSUSA/00001634/201705

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

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Human plasma protease C1 inhibitor - CINRYZE (CAP) - PSUSA/00010104/201706

Applicant: Shire Services BVBA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Hydroxycarbamide¹⁶ - SIKLOS (CAP) - PSUSA/00001692/201706 (with RMP)

Applicant: Addmedica

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Influenza vaccine¹⁷ (live attenuated) - FLUENZ TETRA (CAP) - PSUSA/00001742/201706

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Lesinurad - ZURAMPIC (CAP) - PSUSA/00010470/201706

Applicant: Grunenthal GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁶ For centrally authorised product only

¹⁷ Intranasal use

6.1.30. Levofloxacin¹⁸ - QUINSAIR (CAP) - PSUSA/00010429/201705

Applicant: Chiesi Orphan B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Lonococog alfa - AFSTYLA (CAP) - PSUSA/00010559/201707

Applicant: CSL Behring GmbH

PRAC Rapporteur: Daniela Philadelphly

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Matrix-applied characterised autologous cultured chondrocytes - MACI (CAP) - PSUSA/00010116/201706

Applicant: Vericel Denmark ApS, ATMP¹⁹

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.33. Migalastat - GALAFOLD (CAP) - PSUSA/00010507/201705

Applicant: Amicus Therapeutics UK Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Mirabegron - BETMIGA (CAP) - PSUSA/00010031/201706

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - VELPHORO (CAP) - PSUSA/00010296/201705

Applicant: Vifor Fresenius Medical Care Renal Pharma France

¹⁸ Centrally authorised product only

¹⁹ Advanced therapy medicinal product

PRAC Rapporteur: Julie Williams
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.36. [Nivolumab - OPDIVO \(CAP\) - PSUSA/00010379/201707](#)

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

6.1.37. [Nonacog gamma - RIXUBIS \(CAP\) - PSUSA/00010320/201706](#)

Applicant: Baxalta Innovations GmbH
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.38. [Obeticholic acid - OCALIVA \(CAP\) - PSUSA/00010555/201706](#)

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

6.1.39. [Olaparib - LYNPARZA \(CAP\) - PSUSA/00010322/201706](#)

Applicant: AstraZeneca AB
PRAC Rapporteur: Carmela Macchiarulo
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.40. [Opicapone - ONGENTYS \(CAP\) - PSUSA/00010516/201706](#)

Applicant: Bial - Portela & C^a, S.A.
PRAC Rapporteur: Dolores Montero Corominas
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.41. [Pertuzumab - PERJETA \(CAP\) - PSUSA/00010125/201706](#)

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. [Selexipag - UPTRAVI \(CAP\) - PSUSA/00010503/201706](#)

Applicant: Actelion Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. [Sofosbuvir - SOVALDI \(CAP\) - PSUSA/00010134/201706](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. [Sofosbuvir, velpatasvir - EPCLUSA \(CAP\) - PSUSA/00010524/201706](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. [Sonidegib - ODOMZO \(CAP\) - PSUSA/00010408/201706](#)

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. [Tasimelteon - HETLIOZ \(CAP\) - PSUSA/00010394/201707](#)

Applicant: Vanda Pharmaceuticals Ltd.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Tedizolid phosphate - SIVEXTRO (CAP) - PSUSA/00010369/201706

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Tigecycline - TYGACIL (CAP) - PSUSA/00002954/201706

Applicant: Pfizer Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Trametinib - MEKINIST (CAP) - PSUSA/00010262/201705

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Varenicline - CHAMPIX (CAP) - PSUSA/00003099/201705

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Venetoclax - VENCLYXTO (CAP) – PSUSA/00010556/201706

Applicant: AbbVie Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)

6.2.1. Human normal immunoglobulin (IgG) - FLEBOGAMMA DIF (CAP); HIZENTRA (CAP); HYQVIA (CAP); KIOVIG (CAP); PRIVIGEN (CAP); NAP - PSUSA/00001633/201705

Applicants: Baxalta Innovations GmbH (HyQvia), Baxter AG (Kiovig), CSL Behring GmbH (Hizentra, Privigen), Instituto Grifols, S.A. (Flebogamma DIF), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Lutetium (¹⁷⁷Lu) chloride - ENDOLUCINBETA (CAP); LUMARK (CAP); NAP - PSUSA/00010391/201706

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

PRAC Rapporteur: Almath Spooner

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. Alteplase (NAP) - PSUSA/00000112/201705

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Amlodipine, candesartan (NAP) - PSUSA/00010191/201704

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Amlodipine, olmesartan (NAP) - PSUSA/00002208/201704

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. [Amlodipine besilate, hydrochlorothiazide, olmesartan medoxomil \(NAP\) - PSUSA/00002210/201704](#)

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. [Azithromycin²⁰ \(NAP\) - PSUSA/00010492/201704](#)

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. [Azithromycin²¹ \(NAP\) - PSUSA/00010491/201704](#)

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. [Betaxolol \(NAP\) - PSUSA/00000401/201705](#)

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. [Bismuth subcitrate potassium, metronidazole, tetracycline \(NAP\) - PSUSA/00010199/201705](#)

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

²⁰ Formulations for ocular use only

²¹ Formulations for systemic use only

Action: For adoption of recommendation to CMDh

6.3.9. [Buspirone \(NAP\) - PSUSA/00000463/201704](#)

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. [Candesartan \(NAP\); candesartan, hydrochlorothiazide \(NAP\) - PSUSA/00000527/201704](#)

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. [Chlorpromazine \(NAP\) - PSUSA/00000715/201705](#)

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. [Cidofovir \(NAP\) - PSUSA/00010558/201706](#)

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. [Clevipidine \(NAP\) - PSUSA/00010288/201705](#)

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. [Cyproterone, ethinylestradiol \(NAP\) - PSUSA/00000906/201705](#)

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. [Diltiazem \(NAP\) - PSUSA/00001084/201705](#)

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. [Eprosartan \(NAP\) - PSUSA/00001243/201704](#)

Applicant(s): various

PRAC Lead: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. [Eprosartan, hydrochlorothiazide \(NAP\) - PSUSA/00001244/201704](#)

Applicant(s): various

PRAC Lead: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. [Esomeprazole, naproxen \(NAP\) - PSUSA/00001270/201704](#)

Applicant(s): various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. [Estradiol \(NAP\); estradiol, prednisolone²² \(NAP\) - PSUSA/00010441/201704](#)

Applicant(s): various

PRAC Lead: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

²² Cream/balm/emulsion for application in the female genital area, only

6.3.20. Fluorescein²³ (NAP) - PSUSA/00009153/201704

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Folic acid (NAP) - PSUSA/00001459/201706

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Formoterol (NAP) - PSUSA/00001469/201705

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Glimepiride (NAP) - PSUSA/00001534/201706

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Halofantrine (NAP) - PSUSA/00001586/201705

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Human hemin (NAP) - PSUSA/00001629/201705

Applicant(s): various

PRAC Lead: Ghania Chamouni

²³ For systemic use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Human rabies immunoglobulin (NAP) - PSUSA/00001639/201704

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Indobufen (NAP) - PSUSA/00001736/201705

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Irinotecan²⁴ (NAP) - PSUSA/00001783/201705

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Lanreotide (NAP) - PSUSA/00001826/201705

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Methoxyflurane (NAP) - PSUSA/00010484/201705

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

²⁴ All except liposomal formulations

6.3.31. Methyl salicylate, levomenthol (NAP) - PSUSA/00010241/201704

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.32. Methyl salicylate, levomenthol, DL-camphor (NAP) - PSUSA/00010117/201704

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.33. Mifepristone (NAP) - PSUSA/00002060/201705

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.34. Mifepristone, misoprostol (NAP) - PSUSA/00010378/201705

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.35. Misoprostol²⁵ (NAP) - PSUSA/00010353/201705

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.36. Misoprostol²⁶ (NAP) - PSUSA/00010354/201705

Applicant(s): various

PRAC Lead: Doris Stenver

²⁵ Gynaecological indication - labour induction only

²⁶ Gynaecological indication - termination of pregnancy only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.37. Mometasone (NAP) - PSUSA/00002085/201705

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.38. Olodaterol, tiotropium (NAP) - PSUSA/00010489/201705

Applicant(s): various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.39. Olsalazine (NAP) - PSUSA/00002213/201705

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.40. Piracetam (NAP) - PSUSA/00002429/201704

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.41. Risperidone (NAP) - PSUSA/00002649/201705

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.42. Sodium tetradecyl sulfate (NAP) - PSUSA/00002767/201704

Applicant(s): various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.43. [Strontium \(⁸⁹Sr\) chloride \(NAP\) - PSUSA/00002795/201705](#)

Applicant(s): various

PRAC Lead: Kristin Thorseng Kvande

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.44. [Technetium \(^{99m}Tc\) hynic-octetotide \(NAP\) - PSUSA/00010521/201706](#)

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.45. [Technetium \(^{99m}Tc\) tetrofosmin \(NAP\); tetrofosmin \(NAP\) - PSUSA/00002870/201705](#)

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.46. [Tramadol \(NAP\) - PSUSA/00003002/201705](#)

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.47. [Valsartan \(NAP\); valsartan, hydrochlorothiazide \(NAP\) - PSUSA/00010396/201704](#)

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.48. Venlafaxine (NAP) - PSUSA/00003104/201705

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/LEG 041

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a comprehensive annual report for the ongoing study 20090522: a PASS on denosumab global safety assessment among women with postmenopausal osteoporosis (PMO) and men with osteoporosis in multiple observational databases [final report expected in 2023] as requested in the conclusions of PSUSA/00000954/201609 adopted in April 2017

Action: For adoption of advice to CHMP

6.4.2. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/LEG 008.2

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the annual case study report (CSR) of the ongoing osteonecrosis of the jaw (ONJ) registry case study 20101102 as requested in the conclusions of PSUSA/00009119/201609 adopted in April 2017

Action: For adoption of advice to CHMP

6.4.3. Lixisenatide - LYXUMIA (CAP) - EMEA/H/C/002445/LEG 014

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of a cumulative review including a causality assessment of all cases of 'biliary disorders' identified in clinical trials and post-marketing setting, as requested in the conclusions of PSUSA/00010017/201701 adopted in September 2017

Action: For adoption of advice to CHMP

6.4.4. Plerixafor - MOZOBIL (CAP) - EMEA/H/C/001030/LEG 025

Applicant: Genzyme Europe BV

PRAC Rapporteur: Sabine Straus

Scope: Submission of a cumulative review of cases of arrhythmia and discussion on possible mechanism in view of available preclinical data and reports in healthy volunteers, as requested in the conclusions of PSUSA/00002451/201612 adopted in July 2017

Action: For adoption of advice to CHMP

6.4.5. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/LEG 039.3

Applicant: Bayer AG

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's response to LEG 039.2 [cumulative review on cases of liver-related events (hepatotoxicity) as requested in the recommendation of PSUSA/00002653/201509 adopted by PRAC in April 2016], as per the request for supplementary information (RSI) adopted in October 2017

Action: For adoption of advice to CHMP

6.4.6. Turoctocog alfa - NOVOEIGHT (CAP) - EMEA/H/C/002719/LEG 007

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the clinical trial report for study NN7008-3809: safety and efficacy of turoctocog alfa in prevention and treatment of bleeds in paediatric previously untreated patients with haemophilia A, as requested in the recommendation of PSUSA/00010138/201610 adopted by PRAC in June 2017

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)²⁷

7.1.1. Direct acting antivirals (DAAV) indicated for the treatment of hepatitis C: Daclatasvir – DAKLINZA (CAP); dasabuvir - EXVIERA (CAP); elbasvir, grazoprevir – ZEPATIER (CAP); glecaprevir, pibrentasvir – MAVIRET (CAP); ledipasvir, sofosbuvir - HARVONI (CAP); ombitasvir, periteprevir, ritonavir – VIEKIRAX (CAP); simeprevir - OLYSIO (CAP); sofosbuvir – SOVALDI (CAP); sofosbuvir, velpatasvir – EPCLUSA (CAP); sofosbuvir, velpatasvir, voxilaprevir – VOSEVI (CAP) - EMEA/H/N/PSP/J/0056.2

Applicant(s): AbbVie Limited (Exviera, Maviret, Viekirax), Bristol-Myers Squibb Pharma EEIG (Daklinza), Gilead Sciences International Ltd (Eplusa, Harvoni, Sovaldi, Vosevi), Janssen-Cilag International NV (Olysio), Merck Sharp & Dohme Limited (Zepatier)

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to EMEA/H/N/PSP/J/0056.2 [Joint PASS protocol for a prospective,

²⁷ In accordance with Article 107n of Directive 2001/83/EC

non-interventional study evaluating the risk of early recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAAV) therapy compared to HCV-infected patients without previous DAA therapy during routine clinical care with previous successfully treated HCC, as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the December 2017 PRAC meeting

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)²⁸

7.2.1. Alirocumab - PRALUENT (CAP) - EMA/H/C/003882/MEA 019.3

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 019.2 including revised protocol (version 3) [protocol for a drug utilisation study (DUS) of alirocumab in Europe to assess the effectiveness of the dosing recommendation to avoid very low low-density lipoprotein (LDL)-C levels (study OBS14697)], as per the request for supplementary information (RSI) adopted in April 2017

Action: For adoption of advice to CHMP

7.2.2. Apremilast - OTEZLA (CAP) - EMA/H/C/003746/MEA 005.2

Applicant: Celgene Europe Limited

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 005.1 [PASS protocol in order to collect long-term data using the British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR) psoriatic arthritis (PsA) registry 'BSRBR PsA registry': a disease registry in the EU for PsA and psoriasis] as per the request for supplementary information (RSI) adopted in July 2017

Action: For adoption of advice to CHMP

7.2.3. Avelumab - BAVENCIO (CAP) - EMA/H/C/004338/MEA 002

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Doris Stenver

Scope: Protocol for a non-interventional cohort study to assess the characteristics and management of patients with Merkel cell carcinoma in Germany (listed as a category 3 study in the RMP) [final report expected in Q1 2024] (from initial opinion/MA)

Action: For adoption of advice to CHMP

²⁸ 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

7.2.4. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 002.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 002 [PASS protocol for study I4V-MC-B003: a prospective observational US post-marketing registry study to assess the long-term safety of baricitinib compared with other therapies used in the treatment of adults with moderate-to-severe rheumatoid arthritis in the course of routine clinical care [final report due date: March 2031] (from initial opinion/MA)] as per the request for supplementary information (RSI) adopted at the September 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.2.5. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/MEA 002

Applicant: Leo Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: Protocol (version 1.0) for study NIS-KYNTHEUM-1345: an observational PASS of suicidal behaviour, serious infections, major adverse cardiovascular events (MACE) and malignancy in psoriasis patients treated with brodalumab. The brodalumab assessment of hazards: a multinational safety (BRAHMS) study in electronic healthcare databases [final report expected in Q3 2030] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.6. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/MEA 002

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Protocol for a long-term PASS: 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 [final report expected in Q2 2034] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.7. Conestat alfa - RUCONEST (CAP) - EMEA/H/C/001223/MEA 019.1

Applicant: Pharming Group N.V

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 019 including a revised protocol (version 1.0) [survey to measure the effectiveness of risk minimisation materials distributed to treatment centres/prescribing physicians] as adopted in July 2017

Action: For adoption of advice to CHMP

7.2.8. Dexamethasone - OZURDEX (CAP) - EMEA/H/C/001140/MEA 020.1

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 020 [protocol for a survey to evaluate the physician education component of the simplified Ozurdex (dexamethasone) educational materials in order to assess the effectiveness of the educational material provided to physicians treating patients with Ozurdex by evaluating the physicians' knowledge and understanding of the key information in the Ozurdex injector's guide] as per the request for supplementary information (RSI) adopted at the October 2017 meeting

Action: For adoption of advice to CHMP

7.2.9. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 009.1

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA-009 [PASS protocol for study 109MS303: a dose-blind, multicentre, extension study to determine the long-term safety and efficacy of two doses of BG00012 monotherapy in subjects with relapsing-remitting multiple sclerosis (ENDORSE) [final clinical study report expected in Q1 2024] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.2.10. Eluxadoline - TRUBERZI (CAP) - EMEA/H/C/004098/MEA 005.2

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA-005.1 including a revised protocol (version 1.2) [PASS protocol for study EVM-19596-00-001: a drug utilisation study (DUS) (RMP category 3) using relevant healthcare databases at two different time periods in order to define the compliance to contraindications over time and the number of subjects diagnosed with pancreatitis after eluxadoline treatment] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.2.11. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 003.3

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Amendment to the previously agreed protocol for a drug utilisation study (DUS) to describe baseline characteristics and utilisation patterns of EU patients initiating Duavive or oestrogen + progestin combination hormone replacement therapy (HRT), DUS B2311061, adopted in May 2016

Action: For adoption of advice to CHMP

7.2.12. [Idelalisib - ZYDELIG \(CAP\) - EMEA/H/C/003843/MEA 015.2](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 015.1 including a revised protocol (version 1.2) [PASS protocol for study GS-EU-313-4172: a non-interventional study to assess the safety profile of idelalisib in patients with refractory follicular lymphoma (FL)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.2.13. [Insulin human - INSUMAN \(CAP\) - EMEA/H/C/000201/MEA 047.4](#)

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Amendment to the protocol of the HUBIN registry PASS: a European observational cohort of patients with type 1 diabetes mellitus (T1DM) treated via intraperitoneal route with Insuman Implantable 400 IU/mL in MedtronicMiniMed implantable pump, and an amended statistical analysis plan (SAP) following phase out process of the pump manufacturer for Insuman, previously agreed in May 2017

Action: For adoption of advice to CHMP

7.2.14. [Mirabegron - BETMIGA \(CAP\) - EMEA/H/C/002388/MEA 009.1](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to MEA 009 [Protocol for PASS study 178-PV-002: a drug utilisation study (DUS) of Betmiga (mirabegron) using real-world healthcare databases from the Netherlands, Spain, United Kingdom and Finland] as per the request for supplementary information (RSI) adopted in July 2017

Action: For adoption of advice to CHMP

7.2.15. [Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA \(CAP\) - EMEA/H/C/003687/MEA 004.4](#)

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 004.3 including a revised protocol [PASS protocol for study NB-452: a cross-sectional survey to evaluate the effectiveness of the physician prescribing checklist (PPC) among physicians in the EU] as per the request for supplementary information (RSI) adopted in October 2017

Action: For adoption of advice to CHMP

7.2.16. [Plasmodium falciparum and hepatitis B vaccine \(recombinant, adjuvanted\) - MOSQUIRIX \(Art 58²⁹\) - EMEA/H/W/002300/MEA 002](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: PASS protocol for study EPI-MAL-002 to estimate the incidence of adverse events of special interest (AESI) of meningitis and of other adverse events (AE) leading to hospitalisation or death, in children, prior to implementation of Mosquirix (RTS, S/AS01E) (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.17. [Plasmodium falciparum and hepatitis B vaccine \(recombinant, adjuvanted\) - MOSQUIRIX \(Art 58³⁰\) - EMEA/H/W/002300/MEA 003](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: PASS protocol for study EPI-MAL-003 to estimate the incidence of protocol-defined potential adverse events of special interest (AESI) and other adverse events leading to hospitalisation or death, in children vaccinated with Mosquirix (RTS, S/AS01E) (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.18. [Plasmodium falciparum and hepatitis B vaccine \(recombinant, adjuvanted\) - MOSQUIRIX \(Art 58³¹\) - EMEA/H/W/002300/MEA 015](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: PASS protocol for study EPI-MAL-010: a phase 4, longitudinal, cross-sectional, retrospective, ancillary epidemiology study of the EPI-MAL-005 study to evaluate the genetic diversity in the Plasmodium falciparum parasite circumsporozoite sequences before and after the implementation of the Mosquirix (RTS, S/AS01E) vaccine in malaria-positive subjects ranging from 6 months to less than 5 years of age (from variation II/20)

Action: For adoption of advice to CHMP

7.2.19. [Ustekinumab - STELARA \(CAP\) - EMEA/H/C/000958/MEA 045](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

²⁹ 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)

³⁰ 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)

³¹ 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)

Scope: Protocol for study RRA-20745: a PASS to investigate the long-term safety in adult patients with moderately to severely active Crohn's disease

Action: For adoption of advice to CHMP

7.2.20. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.2

Applicant: AbbVie Limited

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 002.1 including a revised protocol [registry protocol for a prospective observational study P16-562 to assess the long term safety profile of venetoclax in a Swedish cohort of chronic lymphocytic leukaemia (CLL) patients] as per the request for supplementary information (RSI) adopted at the October 2017 meeting

Action: For adoption of advice to CHMP

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

None

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

7.4.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/II/0116/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of: 1) submission of the final report for study IM101537 (listed as a category 3 study in the RMP): a non-interventional healthcare professionals (HCP)/patient cross-sectional survey and retrospective chart review PASS to evaluate the effectiveness of the patient alert card for both intravenous (IV) and subcutaneous (SC) abatacept in a sample of EU countries; 2) submission of an updated RMP (version 24) in order to reflect the early closure of study IM101212 (listed as a category 3 study in the RMP): a post-marketing observational study assessing the long-term safety of abatacept using the DREAM database in the Netherlands. The MAH took the opportunity to introduce further administrative changes in the RMP

Action: For adoption of PRAC Assessment Report

7.4.2. Afatinib - GIOTRIF (CAP) - EMEA/H/C/002280/II/0025

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 1200.217 (listed as a category 3 study in the RMP): a phase 4 study to assess the efficacy and safety of afatinib as second-line therapy for patients with locally advanced or metastatic non-small cell lung cancer

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

³³ In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

harbouring an epidermal growth factor receptor (EGFR) mutation who have failed first-line treatment with platinum-based chemotherapy. The RMP (version 6.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. [Belimumab - BENLYSTA \(CAP\) - EMEA/H/C/002015/II/0052](#)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report for study HGS1006-C1074 (BEL112234) (listed as a category 3 study in the RMP, in fulfilment of a MEA 012): 'a multicentre, continuation trial of belimumab in subjects with systemic lupus erythematosus (SLE) who completed the phase 3 protocol HGS1006-C1056 or HGS1006-C1057'. The RMP (version 26.0) is updated accordingly. In addition, the MAH took the opportunity to update the RMP regarding study BEL116027: an open-label, non-randomized, 52-week study to evaluate treatment holidays and rebound phenomenon after treatment with belimumab 10 mg/kg in SLE subjects for the due date of the final study report and introduction of protocol changes (reduced study sample size), already agreed in the conclusions of recent procedures MEA 006.4 and MEA 006.5

Action: For adoption of PRAC Assessment Report

7.4.4. [Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD \(CAP\) - EMEA/H/C/002574/II/0087](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report for study GS-EU-236-0141 (listed as a category 3 study in the RMP, in fulfilment of a MEA 006): an observational drug utilisation study (DUS) of Stribild in adults with human immunodeficiency virus 1 (HIV-1) infection

Action: For adoption of PRAC Assessment Report

7.4.5. [Entecavir - BARACLUDE \(CAP\) - EMEA/H/C/000623/II/0053](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final study report for study AI463080: a long-term outcome study (10 years) to assess the rates of malignant neoplasms (all, hepatocellular carcinoma (HCC) and non-HCC), liver-related events of hepatitis B virus (HBV) disease progression and mortality. The RMP (version 14) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. [Fluticasone furoate, vilanterol - RELVAR ELLIPTA \(CAP\) - EMEA/H/C/002673/WS1283/0035, REVINTY ELLIPTA \(CAP\) - EMEA/H/C/002745/WS1283/0031](#)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final report for study 205052 (PRJ2214): a drug utilisation study (DUS) to identify the extent of any off-label prescribing fluticasone furoate/vilanterol (FF/VI) in any dose in children less than 12 years of age; and prescribing of FF/VI 200/25 mcg in patients with a diagnosis of chronic obstructive pulmonary disease (COPD) considering the presence of a concurrent diagnosis of asthma. The RMP (version 9.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. [Interferon beta-1b - BETAFERON \(CAP\) - EMEA/H/C/000081/II/0118](#)

Applicant: Bayer AG

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report for study BETAPAEDIC (listed as a category 3 study in the RMP): a non-interventional study evaluating safety and tolerability of Betaferon (interferon beta-1b) in paediatric patients with multiple sclerosis. The RMP (version 3.2) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. [Micafungin - MYCAMINE \(CAP\) - EMEA/H/C/000734/II/0035](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report for the online survey for EU PAS register number EUPAS13634 measuring the effectiveness of the Mycamine prescriber checklist in the EU. The RMP (version 18.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.9. [Moroctocog alfa - REFACTO AF \(CAP\) - EMEA/H/C/000232/II/0142](#)

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: Submission of the final study report for study B1831016 (listed as a category 3 in the RMP, in fulfilment of MEA 108.3: a non-interventional open-label study conducted at haemophilia treatment centres in Germany and Austria to generate information regarding the safety and effectiveness of treatment with ReFacto AF under routine clinical conditions

Action: For adoption of PRAC Assessment Report

7.4.10. Octocog alfa - ADVATE (CAP) - EMEA/H/C/000520/II/0089

Applicant: Baxter AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report for study 061501: a retrospective chart review aimed to evaluate safety and tolerability of Advate among previously untreated patients with moderate to severe haemophilia A

Action: For adoption of PRAC Assessment Report

7.4.11. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - SYNFLORIX (CAP) - EMEA/H/C/000973/II/0124/G

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations consisting of the submission of the final study reports from two 5-year invasive pneumococcal disease (IPD) post-marketing surveillance (PMS) studies: 1) 'monitoring the population effectiveness of pneumococcal conjugate vaccination in the Finnish national vaccination programme' (MEA 019); 2) 'epidemiology of invasive pneumococcal disease in the Netherlands' (MEA 020), addressing the potential risks of 'possible serotype replacement of disease isolates' and 'possible breakthrough infections/vaccine failure'. The MAH also provided data from IPD surveillance from 5 other European countries (Austria, Bulgaria, Cyprus, Iceland and Sweden) and 6-year update results from a 5-year PMS in Kenya (pneumococcal conjugate vaccine impact study (PCVIS), MEA 021). The RMP (version 17) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.12. Zoledronic acid - ACLASTA (CAP) - EMEA/H/C/000595/II/0069

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final 5-year report for study ZOL446H2422 (listed as a category 3 study in the RMP): a non-interventional post-authorisation safety study using health registries to compare safety of Aclasta against oral bisphosphonates and untreated population controls

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. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/MEA 010.2

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

Scope: Third interim results (semi-annual report) for study TMC207TBC4002: a multi-

country prospective multidrug-resistant tuberculosis (MDRTB) disease registry to monitor bedaquiline safety, utilisation, and emergence of resistance (listed as a category 3 study in RMP) [final study report expected in Q2 2020]

Action: For adoption of advice to CHMP

7.5.2. [Dolutegravir - TIVICAY \(CAP\) - EMEA/H/C/002753/MEA 001.2](#)

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 001.1 [Second interim annual report for EuroSIDA PASS study 201177: a prospective observational cohort study in patients receiving dolutegravir (category 3) to investigate the risk of hypersensitivity reactions (HSR), hepatotoxicity and serious rash (division of acquired immune deficiency syndrome (DAIDS) grading scale category 3 or 4)] as per the request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

7.5.3. [Dolutegravir, abacavir, lamivudine - TRIUMEQ \(CAP\) - EMEA/H/C/002754/MEA 007.2](#)

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 007.1 [Second interim annual report for EuroSIDA PASS study 201177: a prospective observational cohort study in patients receiving dolutegravir (category 3) to investigate the risk of hypersensitivity reactions (HSR), hepatotoxicity and serious rash (division of acquired immune deficiency syndrome (DAIDS) grading scale category 3 or 4)] as per the request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

7.5.4. [Edoxaban - LIXIANA \(CAP\) - EMEA/H/C/002629/MEA 005.4](#)

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: Interim study report for study DSE-EDO-01-14-EU (EUPAS17062): a drug utilisation study (DUS), multinational, multicentre involving a retrospective chart review of edoxaban users' medical records. Nested in the study, a cross-sectional survey of all participating prescribing physicians is performed, starting from the date of the first data abstraction and repeated over the course of the study to evaluate the effectiveness of the physician educational programme

Action: For adoption of advice to CHMP

7.5.5. [Etravirine - INTELENCE \(CAP\) - EMEA/H/C/000900/MEA 049.2](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Caroline Laborde

Scope: Fourth annual report for study TMC125-EPPICC: 'a study to define the long-term safety profile of etravirine in human immunodeficiency virus 1 (HIV-1) infected children and adolescents in Europe'

Action: For adoption of advice to CHMP

7.5.6. [Florbetapir \(¹⁸F\) - AMYVID \(CAP\) - EMEA/H/C/002422/MEA 001.4](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: First interim report for study I6E-MC-AVBE: a non-interventional PASS evaluating the effectiveness of Amyvid reader training programme

Action: For adoption of advice to CHMP

7.5.7. [Human papillomavirus vaccine \[types 6, 11, 16, 18, 31, 33, 45, 52, 58\] \(recombinant, adsorbed\) - GARDASIL 9 \(CAP\) - EMEA/H/C/003852/MEA 003](#)

Applicant: MSD Vaccins

PRAC Rapporteur: Julie Williams

Scope: Second annual interim report for an US pregnancy registry: surveillance programme procedures for the pregnancy registry for Gardasil 9

Action: For adoption of advice to CHMP

7.5.8. [Infliximab - REMICADE \(CAP\) - EMEA/H/C/000240/MEA 089.13](#)

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim study reports for the ENCORE patient registry in Europe in Crohn's disease, using data from the Swedish biologics register (anti-rheumatic therapy in Sweden: ARTIS) and the German rheumatoid arthritis observation of biologic therapy (RABBIT) cohort 2

Action: For adoption of advice to CHMP

7.5.9. [Influenza vaccine \(live attenuated, nasal\) - FLUENZ TETRA \(CAP\) - EMEA/H/C/002617/MEA 004.8](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 004.7 [annual interim report for the passive enhanced safety surveillance study (ESS) D2560C00008: a postmarketing non-interventional cohort study of the safety of live attenuated influenza vaccine (LAIV) in subjects 2 through 17

years of age early 2016/2017 influenza season in England] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.5.10. Lipegfilgrastim - LONQUEX (CAP) - EMEA/H/C/002556/MEA 004.4

Applicant: Sicor Biotech UAB

PRAC Rapporteur: Patrick Batty

Scope: Interim results for study XM22-ONC-50002: a multi-country, multicentre, retrospective observational drug utilisation study (DUS) to describe the pattern of lipegfilgrastim use and specifically to quantify the extent of lipegfilgrastim off-label use in routine clinical practice in several countries in the European Union (EU)

Action: For adoption of advice to CHMP

7.5.11. Nalmefene - SELINCRO (CAP) - EMEA/H/C/002583/MEA 003.2

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Martin Huber

Scope: Interim (baseline) report for PASS 15649A: a cohort study on the use of Selincro (nalmefene) using longitudinal electronic medical records or claims databases in Europe (reports from the German, UK and Swedish databases)

Action: For adoption of advice to CHMP

7.5.12. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/ANX 001.4

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

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

Action: For adoption of advice to CHMP

7.5.13. Perampanel - FYCOMPA (CAP) - EMEA/H/C/002434/MEA 004.6

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Julie Williams

Scope: Annual interim analysis for PASS study E2007-G000-402: a post-marketing observational safety study to evaluate the long-term safety and tolerability of Fycompa

(perampanel) as add-on therapy in epilepsy patients

Action: For adoption of advice to CHMP

7.5.14. Roflumilast - DALIRESP (CAP) - EMEA/H/C/002398/ANX 002.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: First interim results for PASS D7120R00003 (previously RO-2455-403-RD): a long-term post-marketing observational study exploring the safety of roflumilast in the treatment of chronic obstructive pulmonary disease (COPD), combined data results from Sweden, Germany and the US [final clinical study report (CSR) expected in March 2031]

Action: For adoption of advice to CHMP

7.5.15. Roflumilast - DAXAS (CAP) - EMEA/H/C/001179/ANX 002.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: First interim results for PASS D7120R00003 (previously RO-2455-403-RD): a long-term post-marketing observational study exploring the safety of roflumilast in the treatment of chronic obstructive pulmonary disease (COPD), combined data results from Sweden, Germany and the US [final clinical study report (CSR) expected in March 2031]

Action: For adoption of advice to CHMP

7.5.16. Roflumilast - LIBERTEK (CAP) - EMEA/H/C/002399/ANX 002.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: First interim results for PASS D7120R00003 (previously RO-2455-403-RD): a long-term post-marketing observational study exploring the safety of roflumilast in the treatment of chronic obstructive pulmonary disease (COPD), combined data results from Sweden, Germany and the US [final clinical study report (CSR) expected in March 2031]

Action: For adoption of advice to CHMP

7.5.17. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/MEA 003.5

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

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

Action: For adoption of advice to CHMP

7.5.18. Valproate – EMEA/H/N/PSI/J/0002

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

PRAC Rapporteur: Sabine Straus

Scope: MAH's response to PSI/J/0002 [second interim results report for a joint drug utilisation study (DUS) of valproate and related substances conducted in Europe aiming at describing the prescribing practices before and after the dissemination of risk minimisation measures (RMM) (i.e. educational materials and direct healthcare professional communication (DHPC)) and assessing the effectiveness of these measures using databases, as requested in the outcome of the referral procedure on valproate and related substances (EMA/H/A-31/1387) concluded in 2014] as per the request for supplementary information (RSI) adopted at the October 2017 meeting

Action: For adoption of conclusions (or request for supplementary information (RSI))

7.6. Others

7.6.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/LEG 101

Applicant: AbbVie Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a further review on exposure and sensitivity analysis, on missing data and on Cox regression analysis related to the final study report for the biologics registry: Anti-Rheumatic Treatment in Sweden (ARTIS), as requested in the conclusions of variation II/061/G adopted by CHMP/PRAC in May 2017

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 006.8

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: Bi-annual status reports for study DNE3001/CREDENCE: a randomised, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with type 2 diabetes mellitus and diabetic nephropathy) from the Independent Data Monitoring Committee (IDMC) (sixth IDMC report dated October 2017)

Action: For adoption of advice to CHMP

7.6.3. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 005.8

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Bi-annual status reports for study DNE3001/CREDENCE: a randomised, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with type 2 diabetes mellitus and diabetic

nephropathy) from the Independent Data Monitoring Committee (IDMC) (sixth IDMC report dated October 2017)

Action: For adoption of advice to CHMP

7.6.4. Cariprazine - REAGILA (CAP) - EMEA/H/C/002770/MEA 005

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Protocol for a PASS RGH-188-303: a randomized, open-label, ophthalmologist-masked study in approximately 1,000 schizophrenic patients to compare lens opacity changes during long-term treatment with cariprazine versus risperidone (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.6.5. Daclatasvir - DAKLINZA (CAP) - EMEA/H/C/003768/MEA 019.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 019 [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.6.6. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/MEA 007.1

Applicant: AbbVie Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to MEA 007 [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.6.7. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/MEA 004.1

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 004 [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.6.8. Glecaprevir, pibrentasvir - MAVIRET (CAP) - EMA/H/C/004430/MEA 006

Applicant: AbbVie Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.6.9. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMA/H/C/003850/MEA 017.1

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 017 [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.6.10. Lopinavir, ritonavir - KALETRA (CAP) - EMA/H/C/000368/LEG 121

Applicant: AbbVie Limited

PRAC Rapporteur: Caroline Laborde

Scope: Submission of an assessment of the safety in children aged from 14 days to 2 years as regards to the chronic exposure to propylene glycol and ethanol, medication errors and lack of efficacy/resistance in relation to potentially suboptimal pharmacokinetic (PK) parameters, together with a discussion on the benefit/risk balance in this population and a discussion on the feasibility to search and identify for any case report of medication error, overdose and lack of efficacy reported in children aged between 14 days and 2 years

receiving Kaletra oral solution based on existing paediatric cohorts, as requested in the conclusions of variation II/061/G adopted by CHMP/PRAC in June 2017

Action: For adoption of advice to CHMP

7.6.11. [Ombitasvir, paritaprevir, ritonavir - VIEKIRAX \(CAP\) - EMEA/H/C/003839/MEA 007.1](#)

Applicant: AbbVie Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to MEA 007 [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.6.12. [Simeprevir - OLYSIO \(CAP\) - EMEA/H/C/002777/MEA 013.1](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 013 [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.6.13. [Sofosbuvir - SOVALDI \(CAP\) - EMEA/H/C/002798/MEA 024.1](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 024 [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.6.14. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/MEA 008.1

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 008 [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.6.15. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/MEA 002

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response [Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 meeting

Action: For adoption of advice to CHMP

7.6.16. Telavancin - VIBATIV (CAP) - EMEA/H/C/001240/ANX 007.6

Applicant: Theravance Biopharma Ireland Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's response to ANX 007.5 [Submission of a pregnancy exposure follow-up questionnaire in the context of the pregnancy exposure registry (9809-CL-1409)] as per the request for supplementary information (RSI) adopted in July 2017

Action: For adoption of advice to CHMP

7.6.17. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/MEA 014

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Submission of primary analysis for study MO28231 (KAMILLA): a two-cohort, open label, multicentre, study of trastuzumab emtansine in human epidermal growth factor (HER2) positive locally advanced or metastatic breast cancer patients who have received prior anti-HER2 and chemotherapy-based treatment [final clinical study report expected in Q4 2021]

Action: For adoption of advice to CHMP

7.6.18. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/LEG 032

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a detailed analysis of a case of hypotension (KW-C14004-17-00092) including the CIOMS³⁴ form, causality assessment report

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

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

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0009 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0026 (without RMP)

Applicant: Aegerion Pharmaceuticals Limited

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

³⁴ Council for International Organisations of Medical Sciences

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/R/0024 (without RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0027 (with RMP)

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Julie Williams

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/R/0007 (without RMP)

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Almath Spooner

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Pixantrone - PIXUVRI (CAP) - EMEA/H/C/002055/R/0042 (without RMP)

Applicant: CTI Life Sciences Limited

PRAC Rapporteur: Patrick Batty

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Matrix applied characterised autologous cultured chondrocytes - MACI (CAP) - EMEA/H/C/002522/R/0017 (with RMP)

Applicant: Vericel Denmark ApS, ATMP³⁵

PRAC Rapporteur: Julie Williams

³⁵ Advanced therapy medicinal product

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.3.2. Sodium phenylbutyrate - PHEBURANE (CAP) - EMEA/H/C/002500/R/0017 (without RMP)

Applicant: Lucane Pharma

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Imatinib – IMATINIB ACCORD (CAP) - EMEA/H/C/002681/R/0020

Applicant: Accord Healthcare Limited

PRAC Rapporteur: Eva Segovia

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. General anaesthetics and sedative medicines: Desflurane (NAP); enflurane (NAP); etomidate (NAP); esketamine (NAP); halothane (NAP); isoflurane (NAP); ketamine (NAP); midazolam – BUCCOLAM (CAP), NAP; propofol (NAP); sevoflurane (NAP); thiopental (NAP)

Applicants: Shire Services BVBA (Buccolam); various

PRAC Lead: Ghania Chamouni

Scope: PRAC advice on the scientific relevance to update the product information for general anaesthetics and sedative medicines regarding the risk of developmental disorders when used in children and pregnant women, in light of available safety data from preclinical and clinical studies, FDA action taken in April 2017, and national variations submitted for isoflurane-, sevoflurane- and propofol-containing medicines, on request of France

Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Chlormadinone acetate, ethinylestradiol (NAP)

Applicants: Gedeon Richter Plc.

PRAC Lead: Valerie Strassmann

Scope: PRAC consultation on the progress report assessment of the RIVET-case control (RIVET-CC) study: a non-interventional PASS (EMA/H/N/PSP/J/0012) imposed following the completion in 2013 of a referral procedure under Article 31 of Directive 2001/83/EC (EMA/607314/2013) for the review of combined hormonal contraceptives (CHCs). The study aims at assessing the risk of venous thromboembolism, (VTE) associated with

chlormadinone acetate (CMA) containing combined oral contraceptives (COCs) compared to levonorgestrel (LNG) containing COCs in a large case-control study, on request of Germany

Action: For adoption of advice to Member States

11.2.2. Levothyroxine (NAP) – DE/H/XXXX/WS/356

Applicant: Merck Serono GmbH (Euthyrox)

PRAC Lead: Valerie Strassmann

Scope: PRAC consultation on the potential issues during the transition period and the need of a communication strategy in the context of a worksharing quality variation for Euthyrox (levothyroxine) on a change in the composition (excipients) of the finished product, on request of Germany

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Scientific advice working party (SAWP) – re-nomination of PRAC representative(s)

Action: For adoption

12.4. Cooperation within the EU regulatory network

12.4.1. Brexit: preparedness of the regulatory network and capacity increase

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2018

PRAC lead: June Raine, Almath Spooner

Action: For adoption

12.8. Planning and reporting

12.8.1. Marketing authorisation applications (MAA) expected for 2018 – Q4 2017 update

Action: For information

12.8.2. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q4 2017 and predictions

Action: For information

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections – union procedure on follow-up of pharmacovigilance inspections

Action: For discussion

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Sabine Straus

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Good Pharmacovigilance Practices (GVP) – revision planned for 2018 - update on GVP status overview

Action: For discussion

12.20.2. Strategy on measuring the impact of pharmacovigilance – final pilot report and work planning 2018

PRAC lead: Valerie Strassmann

Action: For adoption

12.20.3. Codeine - Best evidence pilot study

PRAC lead: Julie Williams, Dolores Montero Corominas

Action: For discussion

13. Any other business

14. Explanatory notes

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

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

(Items 2 and 3 of the PRAC agenda)

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

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WCOB01ac05800240d0

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/