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Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 14-17 May 2018

Chair: June Raine – Vice-Chair: Almath Spooner

14 May 2018, 13:00 – 19:30, room 3/A

15 May 2018, 08:30 – 19:30, room 3/A

16 May 2018, 08:30 – 19:30, room 3/A

17 May 2018, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

31 May 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 14-17 May 2018. See May 2018 PRAC minutes (to be published post June 2018 PRAC meeting).

1.2. Agenda of the meeting on 14-17 May 2018

Action: For adoption

1.3. Minutes of the previous meeting on 09-12 April 2018

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

2.4. Others

2.4.1. 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 PRAC recommendation for a referral procedure under Article 107i of Directive 2001/83/EC adopted in January 2018, following a clarification request of the European Commission

Action: For discussion

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

- 3.2.1. Fluoroquinolones for systemic and inhalation use: ciprofloxacin (NAP); enoxacin (NAP); flumequin (NAP); levofloxacin – QUINSAIR (CAP), NAP; lomefloxacin (NAP); moxifloxacin (NAP); norfloxacin (NAP); ofloxacin (NAP); pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP)
Quinolones for systemic and inhalation use: cinoxacin (NAP); nalidixic acid (NAP); pipemidic acid (NAP) - EMEA/H/A-31/1452

Applicant(s): Raptor Pharmaceuticals Europe BV (Quinsair), various

PRAC Rapporteur: Eva Jirsová; PRAC Co-rapporteur: Martin Huber

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

Action: For discussion on the organisation of the public hearing

3.2.2. Radium (²²³Ra) dichloride - XOFIGO (CAP) - EMEA/H/A-20/1459

Applicant: Bayer AG

PRAC Rapporteur: Patrick Batty; PRAC Co-rapporteur: Valerie Strassmann

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

Action: For adoption of a list of questions (LoQ) and a list of experts (LoE) for an ad-hoc expert group meeting

3.3. Procedures for finalisation

3.3.1. Daclizumab – ZINBRYTA² – EMEA/H/A-20/1462

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia; PRAC Co-rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

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

Action: For adoption of PRAC assessment report

² European Commission (EC) decision on the MA withdrawal of Zinbryta dated 27 March 2018

3.3.2. Ulipristal acetate - ESMYA (CAP) - EMEA/H/A-20/1460

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Menno van der Elst

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

Action: For adoption of a recommendation to CHMP

3.4. Re-examination procedures³

None

3.5. Others

None

4. Signals assessment and prioritisation⁴

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Apixaban – ELIQUIS (CAP)

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

PRAC Rapporteur: Menno van der Elst

Scope: Signal of neutropenia

Action: For adoption of PRAC recommendation

EPITT 19187 – New signal

Lead Member State: NL

4.1.2. 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, paritaprevir, ritonavir - VIEKIRAX (CAP); sofosbuvir - SOVALDI (CAP); sofosbuvir, velpatasvir - EPCLUSA (CAP); sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP)

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

PRAC Rapporteur: To be appointed

Scope: Signal of dysglycaemia

³ Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

⁴ Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

Action: For adoption of PRAC recommendation

EPITT 19234 – New signal

Lead Member States: ES, PT, UK

4.1.3. Dolutegravir – TIVICAY (CAP); abacavir sulfate, dolutegravir sodium, lamivudine – TRIUMEQ (CAP)

Applicant(s): ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

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

Action: For adoption of PRAC recommendation

EPITT 19244 – New signal

Lead Member State: UK

4.1.4. Dulaglutide – TRULICITY (CAP)

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

PRAC Rapporteur: Carmela Macchiarulo

Scope: Signal of acute kidney injury

Action: For adoption of PRAC recommendation

EPITT 19204 – New signal

Lead Member State: IT

4.1.5. Hydroxycarbamide – SIKLOS (CAP), NAP

Applicant(s): Addmedica S.A.S., various

PRAC Rapporteur: To be appointed

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

Action: For adoption of PRAC recommendation

EPITT 19210 – New signal

Lead Member State: BE

4.1.6. Ipilimumab – YERVOY (CAP)

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Signal of cytomegalovirus gastrointestinal infection

Action: For adoption of PRAC recommendation

EPITT 19207 – New signal

Lead Member State: NL

4.1.7. Meningococcal group b vaccine (rDNA, component, adsorbed) – BEXSERO (CAP)

Applicant(s): GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of meningism

Action: For adoption of PRAC recommendation

EPITT 19224 – New signal

Lead Member State: SE

4.1.8. Niraparib – ZEJULA (CAP)

Applicant(s): Tesaro UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Signal of potential occurrence of embolic and thrombotic events

Action: For adoption of PRAC recommendation

EPITT 19206 – New signal

Lead Member State: UK

4.1.9. Nivolumab – OPDIVO (CAP)

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of cholangitis sclerosing

Action: For adoption of PRAC recommendation

EPITT 19203 – New signal

Lead Member State: DE

4.1.10. Teriflunomide – AUBAGIO (CAP)

Applicant(s): Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Signal of dyslipidaemia

Action: For adoption of PRAC recommendation

EPITT 19227 – New signal

Lead Member State: DE

4.1.11. Tocilizumab – ROACTEMRA (CAP)

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of noninfectious encephalitis

Action: For adoption of PRAC recommendation

EPITT 19197 – New signal

Lead Member State: DE

4.1.12. Trastuzumab – HERCEPTIN (CAP), HERZUMA (CAP), ONTRUZANT (CAP); trastuzumab emtansine - KADCYLA (CAP); pertuzumab – PERJETA (CAP)

Applicant(s): Celltrion Healthcare Hungary Kft. (Herzuma), Roche Registration GmbH (Herceptin, Kadcyla, Perjeta), Samsung Bioepis UK Limited (SBUK) (Ontruzant)

PRAC Rapporteur: To be appointed

Scope: Signal of multiple sclerosis relapse

Action: For adoption of PRAC recommendation

EPITT 19208 – New signal

Lead Member States: DE, DK

4.2. New signals detected from other sources

4.2.1. Oxybutynin – KENTERA (CAP), NAP; carbamazepine (NAP)

Applicant(s): Nicobrand Limited (Kentera), various

PRAC Rapporteur: To be appointed

Scope: Signal on drug interaction between oxybutynin and carbamazepine resulting in seizures and carbamazepine overdose secondary to carbamazepine plasma level variations

Action: For adoption of PRAC recommendation

EPITT 19233 – New signal

Lead Member State: BE

4.3. Signals follow-up and prioritisation

4.3.1. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/SDA/030

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 – Follow-up to January 2018

4.3.2. Apixaban – ELIQUIS (CAP) - EMEA/H/C/002148/SDA/031; edoxaban – LIXIANA (CAP) - EMEA/H/C/002629/SDA/010, ROTEAS (CAP) - EMEA/H/C/004339/SDA/002; 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: Julie Williams

Scope: Signal of drug interaction between apixaban or edoxaban and selective serotonin reuptake inhibitors (SSRI) and/or serotonin and noradrenaline reuptake inhibitors (SNRI) leading to increased risk of bleeding

Action: For adoption of PRAC recommendation

EPITT 19139 – Follow-up to January 2018

4.3.3. 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, estradiol⁵ (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, norgestimate 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); ethinylestradiol, gestodene⁶ (NAP); ethinylestradiol, gestodene⁷ (NAP); ethinylestradiol, levonorgestrel (NAP); ethinylestradiol, lynestrenol (NAP); ethinylestradiol, norethisterone (NAP); ethinylestradiol, norgestimate (NAP); ethinylestradiol, norgestrel (NAP); levonorgestrel, ethinylestradiol; ethinylestradiol⁸ (NAP); levonorgestrel (NAP); medroxyprogesterone (NAP); mestranol, norethisterone (NAP); norgestimate (NAP); norgestimate 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: Doris Stenver

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

Action: For adoption of PRAC recommendation

EPITT 19144 – Follow-up to January 2018

4.3.4. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/000717/SDA/049

Applicant(s): Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

⁵ Contraception indication

⁶ All route of administrations except transdermal

⁷ Transdermal application

⁸ Combination pack

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

Action: For adoption of PRAC recommendation

EPITT 19130 – Follow-up to January 2018

4.3.5. [Lenograstim \(NAP\); lipegfilgrastim – LONQUEX \(CAP\); pegfilgrastim – NEULASTA \(CAP\)](#)

Applicant(s): Amgen Europe B.V.(Neulasta), Sicor Biotech UAB (Lonquex), various

PRAC Rapporteur: Patrick Batty

Scope: Signal of pulmonary haemorrhage

Action: For adoption of PRAC recommendation

EPITT 19181 –Follow-up to April 2018

4.3.6. [Pembrolizumab - KEYTRUDA \(CAP\) - EMEA/H/C/003820/SDA/017](#)

Applicant(s): Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Signal of aseptic meningitis

Action: For adoption of PRAC recommendation

EPITT 19115 – Follow-up to January 2018

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. [Binimetinib - EMEA/H/C/004579](#)

Scope: Treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation, in combination with encorafenib

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

5.1.2. [Deferiprone - EMEA/H/C/004710](#)

Scope: Treatment of iron overload in thalassemia major

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

5.1.3. [Durvalumab - EMEA/H/C/004771](#)

Scope: Treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC)

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

5.1.4. [Encorafenib - EMEA/H/C/004580](#)

Scope: Treatment of adult patients with unresectable or metastatic melanoma with a BRAF

V600 mutation, in combination with binimetinib

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

5.1.5. Eravacycline - EMEA/H/C/004237

Scope: Treatment of complicated intra-abdominal infections (cIAI) in adults

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

5.1.6. Gefitinib - EMEA/H/C/004826

Scope: Treatment of non-small cell lung cancer (NSCLC)

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

5.1.7. Glycopyrronium, formoterol fumarate dihydrate - EMEA/H/C/004245

Scope: Maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD)

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

5.1.8. Lenalidomide - EMEA/H/C/004857

Scope: Treatment of multiple myeloma

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

5.1.9. Melatonin - EMEA/H/C/004425, PUMA⁹

Scope: Treatment of insomnia in children with autism spectrum disorders and neurogenetic diseases

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

5.1.10. Meropenem, vaborbactam - EMEA/H/C/004669

Scope: Treatment of complicated urinary tract infection (cUTI), including pyelonephritis, intra-abdominal infection (cIAI), hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP), bacteraemia, infections due to bacterial organisms

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

5.1.11. Mexiletine hydrochloride - EMEA/H/C/004584, Orphan

Applicant: Lupin (Europe) Limited

Scope: Treatment of myotonic disorders

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

⁹ Paediatric-use marketing authorisation(s)

5.1.12. Paclitaxel - EMEA/H/C/004441

Scope: Treatment of metastatic breast cancer

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

5.1.13. Pegfilgrastim - EMEA/H/C/003961

Scope: Treatment of neutropenia

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

5.1.14. Tildrakizumab - EMEA/H/C/004514

Scope: Treatment of adults with moderate-to-severe plaque psoriasis

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

5.1.15. Viable T-cells - EMEA/H/C/002397, Orphan

Applicant: Kiadis Pharma Netherlands B.V., ATMP¹⁰

Scope: Adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

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

5.1.16. Voretigene neparvovec - EMEA/H/C/004451, Orphan

Applicant: Spark Therapeutics Ireland Ltd, ATMP¹¹

Scope: Treatment of patients with vision loss due to Leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy

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

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

5.2.1. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/II/0060

Applicant: Hospira UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Update of the RMP (version 8.0) to introduce the new RMP template, update some milestones of the pharmacovigilance plan and delete some safety concerns from the educational material to healthcare professionals

Action: For adoption of PRAC Assessment Report

¹⁰ Advanced therapy medicinal product

¹¹ Advanced therapy medicinal product

5.2.2. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/II/0051](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Patrick Batty

Scope: Update of the RMP (version 8.0) to introduce the new RMP template, update some milestones of the pharmacovigilance plan and delete some safety concerns from the educational material to healthcare professionals

Action: For adoption of PRAC Assessment Report

5.2.3. [Osimertinib - TAGRISSO \(CAP\) - EMEA/H/C/004124/II/0022](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Update of the RMP (version 9) in order to remove PASS D5165C00001 (a category 3 study in the RMP): 'a phase 3, multicentre, open label, randomized study to assess the efficacy and safety of osimertinib (AZD9291) in combination with durvalumab (MEDI4736) versus osimertinib monotherapy in patients with locally advanced or metastatic epidermal growth factor receptor T790M mutation-positive non-small cell lung cancer who have received prior epidermal growth factor receptor tyrosine kinase inhibitor therapy (CAURAL)' from the pharmacovigilance plan

Action: For adoption of PRAC Assessment Report

5.2.4. [Osimertinib - TAGRISSO \(CAP\) - EMEA/H/C/004124/II/0023](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Update of the RMP (version 9) in order to remove PASS D5160C00022 (a category 3 study in the RMP): 'an open label, multinational, multicentre, real world treatment study of single agent osimertinib for patients with advanced/metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC) who have received prior therapy with an EGFR tyrosine kinase inhibitor (EGFR-TKI) (ASTRIS)' from the pharmacovigilance plan

Action: For adoption of PRAC Assessment Report

5.2.5. [Pregabalin - LYRICA \(CAP\) - EMEA/H/C/000546/WS1364/0092; PREGABALIN PFIZER \(CAP\) - EMEA/H/C/003880/WS1364/0021](#)

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of the RMP (version 12.0) in order to include the changes requested in the conclusions of EMEA/H/C/PSUSA/00002511/201701 procedure finalised in September 2017, updating the safety specifications and risk minimisation measures. The pharmacovigilance plan is also updated. The draft protocol for a non-interventional non-imposed PASS (A0081359) entitled 'a population-based cohort study of pregabalin to characterize pregnancy outcomes' is submitted. The MAH took the opportunity to include minor updates

and to align the RMP to the most recent template (revision 2)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0045

Applicant: Bayer AG

PRAC Rapporteur: Ghania Chamouni

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to add information related to earlier treatment extension and related increments intervals based on the final study results of study ALTAIR: an interventional, randomized, open-label phase 4 study evaluating the efficacy and safety of repeated doses of intravitreal (IVT) aflibercept with variable treatment intervals in Japanese subjects with neovascular age-related macular degeneration (AMD). The package leaflet is updated accordingly. The RMP (version 24.1) is updated accordingly

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

5.3.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0007/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Grouped variations consisting of: 1) extension of indication to include in combination with bevacizumab, paclitaxel and carboplatin the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC), based on the interim results of study GO29436: a phase 3, open-label, randomized study of atezolizumab in combination with carboplatin+paclitaxel with or without bevacizumab compared with carboplatin+paclitaxel +bevacizumab in chemotherapy-naïve patients with stage IV NSCLC (IMpower 150). As a consequence sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated; 2) update of section 4.8 of the SmPC in order to update the monotherapy safety data and reflect the largest pooled monotherapy population available (including data from study IMvigor211: a phase 3, open-label, multicentre, randomized study to investigate the efficacy and safety of atezolizumab compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure with platinum-containing chemotherapy, and study PCD4989g: a phase 1, open-label, dose-escalation study of the safety and pharmacokinetics of atezolizumab administered intravenously as a single agent to patients with locally advanced or metastatic solid tumours or hematologic malignancies). The package leaflet and the RMP (version 4.0) are updated accordingly. In addition, the MAH took the opportunity to make small corrections and formatting changes throughout the SmPC

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/0055, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the frontline treatment of adult patients with

CD30+ advanced Hodgkin lymphoma (HL) in combination with chemotherapy, based on data from ECHELON-1 (C25003): a phase 3 multicentre, randomised, open-label study comparing the modified progression-free survival (mPFS) obtained with brentuximab vedotin, doxorubicin, vinblastine and dacarbazine versus the mPFS obtained with doxorubicin, bleomycin, vinblastine and dacarbazine. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 13) are updated accordingly. Furthermore, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)

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

5.3.4. [Brivaracetam - BRIVIACT \(CAP\) - EMEA/H/C/003898/II/0010/G](#)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped application consisting of: 1) extension of indication to include adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy 4 years of age and older. As a consequence, sections 4.1, 4.2, 4.7, 5.1 and 5.2 of the SmPC are updated; 2) submission of a 5 mL oral syringe and adaptor for the paediatric population. The package leaflet, labelling and the RMP (version 6.1) are updated accordingly. The submission also includes a final environmental risk assessment (ERA) for the inclusion of the paediatric population in accordance with the new proposed indication

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

5.3.5. [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 include the safety and efficacy information on cardiovascular events following the final results from the CANVAS programme consisting of study DIA3008 (CANVAS study): 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 (CANVAS-R study): 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

5.3.6. [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 include the safety and efficacy information on cardiovascular events following the final results from CANVAS programme consisting of study DIA3008 (CANVAS study): 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 (CANVAS-R study): 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

5.3.7. [Trametinib - MEKINIST \(CAP\) - EMEA/H/C/002643/WS1274/0023](#); [Dabrafenib - TAFINLAR \(CAP\) - EMEA/H/C/002604/WS1274/0031](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the combination adjuvant treatment with trametinib and dabrafenib of adult patients with stage III melanoma with a BRAF V600 mutation, following complete resection. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the Mekinist and Tafinlar SmPCs are updated. The package leaflet and the RMP (version 14.0 for Mekinist and version 9.0 for Tafinlar) are updated accordingly. In addition, the MAH took the opportunity to correct some typos throughout the Mekinist and Tafinlar product information, to include a cross reference to the Mekinist SmPC in section 4.6 of the Tafinlar SmPC regarding fertility as well as to update the list of local representatives for Bulgaria, Hungary, Estonia, Latvia and Lithuania in the package leaflet of both products

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

5.3.8. [Dapagliflozin - EDISTRIDE \(CAP\) - EMEA/H/C/004161/WS1344/0025](#); [FORXIGA \(CAP\) - EMEA/H/C/002322/WS1344/0044](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to include the treatment of insufficiently controlled type 1 diabetes mellitus (T1DM) as an adjunct to insulin, when insulin does not provide adequate glycaemic control, for Forxiga and Edistride (dapagliflozin). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet and RMP (version 16) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the SmPC and package leaflet

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

5.3.9. [Darunavir - PREZISTA \(CAP\) - EMEA/H/C/000707/WS1312/0093](#); [Darunavir, cobicistat - REZOLSTA \(CAP\) - EMEA/H/C/002819/WS1312/0023](#); [Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA \(CAP\) - EMEA/H/C/004391/WS1312/0005](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPCs for Prezista, Rezolsta and Symtuza to reflect the data of study TMC114HIV3015 (listed as a category 3 study in the

RMP): a single arm, open label study to assess the pharmacokinetics of darunavir and ritonavir, darunavir and cobicistat, etravirine, and rilpivirine in human immunodeficiency virus-1 (HIV-1) infected pregnant women. The package leaflet of Symtuza and the RMPs (version 25.3 for Prezista, version 4.3 for Rezolsta and version 2.1 for Symtuza) are updated accordingly. In addition, the MAH took the opportunity to implement the RMP template (version 2) for Prezista and Rezolsta RMPs, the removal of the fulfilled category 4 'data collection on adverse events of anti-HIV drugs' (D:A:D) study from the Prezista and Rezolsta RMPs, removal of observational study on growth in children and 'growth abnormalities in the paediatric population' as an important potential risk in the Prezista RMP as well as the addition of the missing information 'safety in patients with cardiac conduction disorders' in the Rezolsta RMP (alignment with Tybost (cobicistat) RMP)

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

5.3.10. Dasatinib - SPRYCEL (CAP) - EMEA/H/C/000709/II/0059

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include a paediatric indication for Philadelphia chromosome positive acute lymphoblastic leukaemia. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 16.0) are updated accordingly. 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

5.3.11. Decitabine - DACOGEN (CAP) - EMEA/H/C/002221/II/0033, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Update of section sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to reflect the results from the paediatric study DACOGENAML2004: a phase 1-2 safety and efficacy study of Dacogen (decitabine) in sequential administration with cytarabine in children with relapsed or refractory acute myeloid leukaemia' as per the requirement of Article 46 of Regulation (EC) No1901/2006. The RMP (version 3.1), in line with the revision 2 of the RMP template, is updated accordingly. In addition, the MAH took the opportunity to update section 4.4 of the SmPC to align the safety warning related to sodium excipient with the Annex to the revised European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. The package leaflet is updated accordingly. Moreover, the contact details of the local representative in Slovenia are updated in the package leaflet

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

5.3.12. Eluxadoline - TRUBERZI (CAP) - EMEA/H/C/004098/II/0005/G

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of: 1) submission of the final report from study ELX-PH-08 (listed as a category 3 study in the RMP). This is an in vitro evaluation study aimed

to investigate the effects on treating primary cultures of cryopreserved human hepatocytes with eluxadoline on the expression of cytochrome P450 (CYP) enzymes; 2) submission of the final report from study 3030-102-002 (listed as a category 3 study in the RMP). This is a randomised, open label study aimed to evaluate the effect of eluxadoline as a potential time dependent inhibitor of CYP3A4¹² with the substrate midazolam. The RMP (version 2.0) is updated to refine the important identified risk of 'sphincter of Oddi (SO) spasm' to 'SO spasm (sphincter of Oddi dysfunction, SOD)' and to include pancreatitis as an important identified risk as agreed in the conclusions of PSUSA/00010528/201703 finalised at PRAC/CHMP in October 2017

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

5.3.13. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/II/0039/G

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) extension of indication to include patients with non-metastatic castration-resistant prostate cancer (CRPC). As a consequence, sections 4.1 and 5.1 of the SmPC are updated based on the supportive clinical study results of study MDV3100-14 (PROSPER): a phase 3 randomized controlled study, designed to investigate the safety and efficacy of enzalutamide in patients with non-metastatic castration-resistant prostate cancer; study MDV3100-09 (STRIVE): a multicentre phase 2 study to investigate the safety and efficacy of enzalutamide versus bicalutamide in men with non-metastatic or metastatic castration-resistant prostate cancer; and based on supportive non-clinical data from 7 new reports. The package leaflet and the RMP (version 12.1) are updated accordingly; 2) update of sections 4.4, 4.7, 4.8 and 5.2 of the SmPC in order to amend the warning on possible association with seizure, the effects on driving or operating machines, the identified adverse reactions and to amend the 'race' subsection regarding pharmacokinetic properties based on the results from the completed study PROSPER and study PREVAIL: a multinational phase 3, randomized, double-blind, placebo-controlled efficacy and safety study of oral enzalutamide in chemotherapy-naive subjects with progressive metastatic prostate cancer who have failed androgen deprivation therapy; as well as the updated integrated clinical safety database. The package leaflet is updated accordingly

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

5.3.14. 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-based pharmacokinetic (Pop-PK) extrapolation model analysis from preclinical MRPO-2015-PKM-005, investigating the drug-drug interaction with azathioprine when co-administered with febuxostat. The RMP (version 6.0) is updated accordingly. In

¹² Cytochrome P 450 3A4

addition, the MAH took the opportunity to correct typing errors 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

5.3.15. [Fidaxomicin - DIFICLIR \(CAP\) - EMEA/H/C/002087/II/0032/G](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the safety information following final results from study ANEMONE listed as an additional pharmacovigilance activity in the RMP: a drug utilisation study (DUS) of the use of oral fidaxomicin in routine clinical settings. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet; 2) update of sections 4.4 and 5.2 of the SmPC in order to update the safety information based on the results from study PROFILE: an open label study designed to evaluate the pharmacokinetics of fidaxomicin in inflammatory bowel disease (IBD) subjects with *Clostridium difficile* infection (CDI). The package leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.16. [Fingolimod - GILENYA \(CAP\) - EMEA/H/C/002202/II/0047](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of the final clinical study report (CSR) for study D2399 (listed as a category 3 study in the RMP): a single arm, open-label, multicentre study evaluating the long-term safety and tolerability study of fingolimod 0.5 mg/day administered orally once daily in approximately 5,000 patients with relapsing multiple sclerosis. The RMP (version 14.0) is updated accordingly

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

5.3.17. [Florbetapir \(¹⁸F\) - AMYVID \(CAP\) - EMEA/H/C/002422/II/0029](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Update of section 4.4 of the SmPC following the final report from study I6E-MC-AVBF (listed as a category 3 study in the RMP): a non-interventional category 3 study, a European drug usage survey to assess the usage pattern of Amyvid (florbetapir (¹⁸F)) in the EU. The RMP (version 3.1) is updated accordingly

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

5.3.18. [Fluticasone furoate, umeclidinium, vilanterol - ELEBRATO ELLIPTA \(CAP\) - EMEA/H/C/004781/WS1369/0001; TRELEGY ELLIPTA \(CAP\) - EMEA/H/C/004363/WS1369/0001](#)

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to modify the current approved chronic obstructive pulmonary disease (COPD) therapeutic indication to 'maintenance treatment in adult patients with moderate to severe COPD'. As a consequence, sections 4.1, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 02) are updated accordingly. This is based on the results of study CTT116855: a phase 3, 52 week, randomized, double-blind, 3-arm parallel group study, comparing the efficacy, safety and tolerability of the fixed dose triple combination fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) with the fixed dose dual combinations of FF/VI and UMEC/VI, all administered once-daily in the morning via a dry powder inhaler in subjects with COPD; study 200812: a phase 3B, 24-week randomised, double-blind study to compare 'closed' triple therapy (FF/UMEC/VI) with 'open' triple therapy (FF/VI + UMEC) in subjects with COPD; and the population pharmacokinetics (PK) report 208059

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

5.3.19. [Human papillomavirus vaccine \[types 6, 11, 16, 18\] \(recombinant, adsorbed\) - GARDASIL \(CAP\) - EMEA/H/C/000703/WS1349/0076/G; SILGARD \(CAP\) - EMEA/H/C/000732/WS1349/0064/G](#)

Applicant: MSD Vaccins

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations consisting of an update of section 5.1 of the SmPC following the final results from two long-term follow-up (LTFU) studies, namely: study V501-020-21 (listed as a category 3 study in the RMP): 1) an extension of study V501-020, the pivotal efficacy study of the quadrivalent human papillomavirus (qHPV) vaccine in young men 16 to 26 years of age, in order to assess the effectiveness and immunogenicity of the qHPV vaccine for up to 10 years of follow-up (fulfilment of Gardasil MEA 070.3 and Silgard MEA 069.3); 2) extension study V501-16: extension of a base study MSD-sponsored randomized clinical trial assessing the immunogenicity of a 2 dose schedule of qHPV in adolescents 9 to 13 years of age compared to a 3-dose schedule in young women 16 to 26 years of age. The study provides additional immunogenicity follow-up through 5 years post-vaccination (fulfilment of Gardasil REC 083 and Silgard REC 080).The RMP (version 12) is updated accordingly. In addition, the MAH took the opportunity to bring the product information (PI) in line with the latest QRD template (version 10)

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

5.3.20. [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

template. The RMP (version 14.1) is updated accordingly

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

5.3.21. [Nivolumab - OPDIVO \(CAP\) - EMEA/H/C/003985/WS1278/0042;](#) [Ipilimumab - YERVOY \(CAP\) - EMEA/H/C/002213/WS1278/0053](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the combination treatment with nivolumab and ipilimumab of adult patients with intermediate/poor-risk advanced renal cell carcinoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Opdivo and Yervoy SmPCs are updated. The package leaflet and the RMP (version 19.0 for Yervoy and version 13.0 for Opdivo) are updated accordingly. In addition, the MAH took the opportunity to correct some typos throughout the Yervoy (ipilimumab) and Opdivo (nivolumab) product information

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

5.3.22. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/II/0063/G, Orphan](#)

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Grouped variations consisting of: 1) extension of indication to include the combination regimen of the ivacaftor 150 mg evening dose and Symkevi (tezacaftor/ivacaftor); to add a blister card pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/005); 2) addition of a blister pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/006). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 6.5 and 8 of the SmPC are updated. Annex A, the package leaflet, labelling and RMP (version 6.0) are updated accordingly

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

5.3.23. [Ledipasvir, sofosbuvir - HARVONI \(CAP\) - EMEA/H/C/003850/II/0064](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of section 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety and efficacy information based on interim results from study GS-US-334-0154 (listed as a category 3 study in the RMP): a study to evaluate the safety, efficacy and pharmacokinetics in patients treated with ledipasvir/sofosbuvir fixed-dose combination for 12 weeks in genotype 1 or 4 hepatitis C virus (HCV)-infected subjects with renal insufficiency. The package leaflet and the RMP (version 3.2) are updated accordingly

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

5.3.24. [Lenalidomide - REVLIMID \(CAP\) - EMEA/H/C/000717/II/0098, Orphan](#)

Applicant: Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Update of Annex II to amend the key elements of the risk minimisation programme with information on prescription duration and to revise due dates of two post-authorisation non-interventional, safety studies CC-5013-MDS-10 and CC-5013-MDS-1 on patients with myelodysplastic syndromes (MDS) treated with lenalidomide to gather safety data on the use of lenalidomide in MDS patients and monitor off-label use. Section 4.4 of the SmPC is updated accordingly. The RMP (version 35) is updated in line with GVP module V on 'Risk management systems' revision 1, in order to reclassify and/or rename known safety concerns associated with the use of Revlimid (lenalidomide). As a consequence, Annex IID is updated

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

5.3.25. 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 4, 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

5.3.26. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0023, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Patrick Batty

Scope: Update of section 5.1 of the SmPC in order to update the overall survival data based on the final results from study BO21004/CLL11 (listed as a category 3 study in the RMP): a pivotal study evaluating the efficacy and safety of obinutuzumab as therapy for patients with previously untreated chronic lymphocytic leukaemia (CLL) with comorbidities. The RMP (version 4.0) is updated accordingly. In addition, the MAH took the opportunity to format the listing of 'other side effects' and correct the term 'heart attack to heart failure' in section 4 of the package leaflet

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

5.3.27. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/II/0002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to include information on

vaccination based on interim results from study BN29739 (listed as a category 3 study in the RMP): a phase 3b, multicentre, randomised, parallel-group, open-label study to evaluate the effects of ocrelizumab on immune response in patients with relapsing forms of multiple sclerosis (MS). The package leaflet and the RMP (version 2.0) are updated accordingly. The RMP version 2.0 has also been submitted

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

5.3.28. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0021

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Update of SmPC sections 4.5, 4.6 and 5.2 to reflect the results of study D5160C00036: undertaken to assess the effect of single and multiple oral doses of osimertinib on the pharmacokinetics of a p-glycoprotein probe drug (fexofenadine) in patients with advanced epidermal growth factor receptor mutated (EGFRm) non-small-cell lung carcinoma (NSCLC) that have progressed on a prior epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKI) regimen. The package leaflet and the RMP (version 9) are updated accordingly. In addition, the MAH took the opportunity to make a minor correction in Annex II and to implement minor editorial and/or QRD template related changes in the SmPC and package leaflet

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

5.3.29. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0024

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.2 and 5.2 of the SmPC based on the results from study D5160C00008 to determine the pharmacokinetics, safety and tolerability of osimertinib following a single oral dose to patients with advanced solid tumours and normal hepatic function or mild or moderate hepatic impairment. The RMP (version 9) is updated accordingly

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

5.3.30. Pegaspargase - ONCASPAR (CAP) - EMEA/H/C/003789/II/0016/G

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Patrick Batty

Scope: Grouped variations consisting of an update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1 5.2 and 5.3 of the SmPC with the final results from 2 studies, namely: 1) study DFCI 11-001 (listed as a category 3 study in the RMP): a phase 2, open-label, randomized, multicentre study to determine the safety and feasibility of administering an investigational asparaginase product (asparaginase formulation) compared with Oncaspar (pegaspargase) in subjects aged 1 to <22 years with newly diagnosed acute lymphoblastic leukaemia (ALL) or lymphoblastic lymphoma; 2) study AALL07P4 (listed as a category 3 study in the RMP): a multicentre, open label, randomized, active-controlled, parallel design clinical pilot study conducted to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), safety,

immunogenicity and efficacy of an investigational asparaginase product in comparison with Oncaspar (pegaspargase) in patients aged 1 to <31 years newly diagnosed with high risk B-precursor ALL. 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

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

Applicant: Genzyme Europe BV

PRAC Rapporteur: Sabine Straus

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

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

5.3.32. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/II/0058

Applicant: Bayer AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to include the prevention of stroke, myocardial infarction and cardiovascular death, and for the prevention of acute limb ischaemia and mortality in adult patients with coronary artery disease (CAD) or peripheral artery disease (PAD) for Xarelto 2.5 mg co-administered with acetylsalicylic acid. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The package leaflet, labelling and the RMP (version 11.1) are updated accordingly. In addition, section 4.8 of the SmPC is updated for all other dose strengths (10/15/20 mg) of Xarelto with relevant exposure information based on the provided clinical data

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

5.3.33. Rufinamide - INOVELON (CAP) - EMEA/H/C/000660/II/0045, Orphan

Applicant: Eisai Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: Extension of indication to include the treatment of seizures associated with Lennox Gastaut syndrome in patients of 1 year of age and older as adjunctive therapy. As a consequence, sections 4.1, 4.2, 4.5, 5.1 and 5.2 are updated. The package leaflet and the RMP (version 10.0) are updated accordingly. In addition, the MAH took the opportunity to include minor corrections in the product information and to update the name and contact details of the local representative in Belgium and Luxembourg. Furthermore, the product information is brought in line with the latest QRD template (version 10)

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

5.3.34. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0033/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include information on dose up-titration for psoriatic arthritis (PsA) and update the radiographic sub-section for PsA based on results from the 24-week data from study CAIN457F2342: a phase 3, randomized, double-blind, placebo controlled multicentre study of subcutaneous secukinumab (150 mg and 300 mg) in prefilled syringe to demonstrate efficacy (including inhibition of structural damage), safety, and tolerability up to 2 years in subjects with active psoriatic arthritis (FUTURE 5), the pooled data from PsA phase 3 studies, the pooled data from patients who up-titrated their secukinumab dose in the following studies, namely: study CAIN457F2306E1: a three-year extension study to evaluate the long term efficacy, safety and tolerability of secukinumab in patients with active PsA; study CAIN457F2312: efficacy at 24 weeks with long term safety, tolerability and efficacy up to 5 years of secukinumab in patients of active psoriatic arthritis (FUTURE 2) as well as study CAIN457F2318: 24 week efficacy and 3-year safety and efficacy of secukinumab in active psoriatic arthritis, and long-term study observations which demonstrate higher rates of discontinuation for patients on secukinumab 150 mg compared to patients on secukinumab 300 mg. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to bring it in line with the latest approved SmPC as per procedure IB/0028 finalised in July 2017; 2) the RMP (version 3.0) is updated to include suicidal ideation and behaviour as an important potential risk in the RMP and including minor administrative/editorial changes (LEG 005.2)

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

5.3.35. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/II/0002/G

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped quality variations. The RMP (version 2.0) is updated accordingly

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

5.3.36. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/X/0005/G

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Grouped variations consisting of: 1) extension application (line extension) to introduce a new strength (10 mg film coated tablets); 2) extension of indication to include 'the induction and maintenance of treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent'. The RMP (version 2.0) is updated accordingly

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

5.3.37. Vemurafenib - ZELBORAF (CAP) - EMEA/H/C/002409/II/0048/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of section 5.3 of the SmPC with information on mean bioavailability of vemurafenib at steady state based on study GO28395: a phase 1, open-label, absolute bioavailability study of vemurafenib in patients with BRAFV600 mutation-positive malignancies; 2) Submission of the clinical study report (CSR) for study GO27826: a phase 3, randomised, double-blind, placebo-controlled study of vemurafenib (RO5185426) adjuvant therapy in patients with surgically resected, cutaneous BRAF-mutant melanoma at high risk for recurrence. The RMP (version 11.0) is updated accordingly. The MAH took the opportunity to include some minor editorial changes have been included in the product information (PI)

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. Arsenic trioxide - TRISENOX (CAP) - PSUSA/00000235/201709

Applicant: Teva B.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Bexarotene - TARGRETIN (CAP) - PSUSA/00000404/201709

Applicant: Eisai Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Bezlotoxumab - ZINPLAVA (CAP) - PSUSA/00010576/201710

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Cariprazine - REAGILA (CAP) - PSUSA/00010623/201712

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Ceftaroline fosamil - ZINFORO (CAP) - PSUSA/00010013/201710

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Ceritinib - ZYKADIA (CAP) - PSUSA/00010372/201710

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Cerliponase alfa - BRINEURA (CAP) - PSUSA/00010596/201710

Applicant: BioMarin International Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Cetuximab - ERBITUX (CAP) - PSUSA/00000635/201709

Applicant: Merck KGaA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - PSUSA/00010590/201710

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - PSUSA/00010449/201711

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Conestat alfa - RUCONEST (CAP) - PSUSA/00000873/201710

Applicant: Pharming Group N.V

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Deferasirox - EXJADE (CAP) - PSUSA/00000939/201710

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Defibrotide - DEFITELIO (CAP) - PSUSA/00010086/201710

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Delamanid - DELTYBA (CAP) - PSUSA/00010213/201710

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Dinutuximab beta - QARZIBA (CAP) - PSUSA/00010597/201711

Applicant: EUSA Pharma (UK) Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Diphtheria (D), tetanus (T), pertussis (whole cell) (Pw) and hepatitis B (rDNA) (HBV) vaccine (adsorbed) - TRITANRIX HB (Art 58¹³) - EMEA/H/W/003838/PSUV/0010

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné; PRAC Co-rapporteur: Brigitte Keller-Stanislawski

¹³ 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 PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.17. [Edoxaban - LIXIANA \(CAP\); ROTEAS \(CAP\) - PSUSA/00010387/201710 \(with RMP\)](#)

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. [Flutemetamol \(¹⁸F\) - VIZAMYL \(CAP\) - PSUSA/00010293/201710](#)

Applicant: GE Healthcare Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. [Granisetron¹⁴ - SANCUSO \(CAP\) - PSUSA/00010101/201710](#)

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. [Idarucizumab - PRAXBIND \(CAP\) - PSUSA/00010435/201710](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. [Iloprost¹⁵ - VENTAVIS \(CAP\) - PSUSA/00001724/201709](#)

Applicant: Bayer AG

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁴ Transdermal patch only

¹⁵ Aerosol only

6.1.22. [Insulin glargine - ABASAGLAR \(CAP\); LANTUS \(CAP\); LUSDUNA \(CAP\); TOUJEO \(CAP\) - PSUSA/00001751/201710](#)

Applicant(s): Eli Lilly Nederland B.V. (Abasaglar), Sanofi-Aventis Deutschland GmbH (Lantus, Toujeo), Merck Sharp & Dohme Limited (Lusduna)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. [Irinotecan¹⁶ - ONIVYDE \(CAP\) - PSUSA/00010534/201710](#)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. [Lurasidone - LATUDA \(CAP\) - PSUSA/00010114/201710](#)

Applicant: Aziende Chimiche Riunite Angelini Francesco S.p.A.

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. [Macitentan - OPSUMIT \(CAP\) - PSUSA/00010115/201710](#)

Applicant: Actelion Registration Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. [Melatonin - CIRCADIN \(CAP\) - PSUSA/00001963/201709](#)

Applicant: RAD Neurim Pharmaceuticals EEC Ltd.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. [Micafungin - MYCAMINE \(CAP\) - PSUSA/00002051/201710](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

¹⁶ Liposomal formulations only

Action: For adoption of recommendation to CHMP

6.1.28. Miglustat - ZAVESCA (CAP) - PSUSA/00002062/201710

Applicant: Actelion Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Nintedanib¹⁷ - VARGATEF (CAP) - PSUSA/00010318/201710

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Agni Kapou

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Nintedanib¹⁸ - OFEV (CAP) - PSUSA/00010319/201710

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Obinutuzumab - GAZYVARO (CAP) - PSUSA/00010279/201710

Applicant: Roche Registration GmbH

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Ocriplasmin - JETREA (CAP) - PSUSA/00010122/201710

Applicant: ThromboGenics NV

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Ofatumumab - ARZERRA (CAP) - PSUSA/00002202/201710

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

¹⁷ Oncology indications only

¹⁸ Respiratory indication only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Olaratumab - LARTRUVO (CAP) - PSUSA/00010541/201710

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) – FOCLIVIA (CAP); prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - PSUSA/00010008/201710

Applicant: Seqirus S.r.l

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Para-aminosalicylic acid¹⁹ - GRANUPAS (CAP) - PSUSA/00010171/201710

Applicant: Lucane Pharma

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Parathyroid hormone - NATPAR (CAP) - PSUSA/00010591/201710

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Pasireotide - SIGNIFOR (CAP) - PSUSA/00009253/201710

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁹ Centrally authorised product(s) only

6.1.39. Patisomer - VELTASSA (CAP) - PSUSA/00010618/201710

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Pazopanib - VOTRIENT (CAP) - PSUSA/00002321/201710

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Posaconazole - NOXAFIL (CAP) - PSUSA/00002480/201710

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Prucalopride - RESOLOR (CAP) - PSUSA/00002568/201710 (with RMP)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Siltuximab - SYLVANT (CAP) - PSUSA/00010254/201710

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Sofosbuvir, ledipasvir - HARVONI (CAP) - PSUSA/00010306/201710

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. Stiripentol - DIACOMIT (CAP) - PSUSA/00002789/201711

Applicant: Biocodex

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Strontium ranelate - OSSEOR (CAP); PROTELOS (CAP) - PSUSA/00009301/201709

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Sulfur hexafluoride - SONOVUE (CAP) - PSUSA/00002822/201709

Applicant: Bracco International B.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/201710

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Thalidomide - THALIDOMIDE CELGENE (CAP) - PSUSA/00002919/201710

Applicant: Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/201711

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Toremifene - FARESTON (CAP) - PSUSA/00002999/201709

Applicant: Orion Corporation

PRAC Rapporteur: Ghania Chamouni

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. Sodium oxybate²⁰ - XYREM (CAP); NAP - PSUSA/00010612/201710

Applicants: UCB Pharma Limited (Xyrem), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Adapalene, benzoyl peroxide (NAP) - PSUSA/00000059/201709

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Bromazepam (NAP) - PSUSA/00000435/201708

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Calcium carbonate, famotidine, magnesium hydroxide (NAP) - PSUSA/00001351/201709

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

²⁰ Oral use only

6.3.4. Dermatophagoides pteronyssinus, dermatophagoides farina²¹ (NAP) - PSUSA/00010582/201709

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Desflurane (NAP) - PSUSA/00000958/201709

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Dexibuprofen (NAP) - PSUSA/00000996/201708

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Dornase alfa (NAP) - PSUSA/00001164/201709

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Etidronate (NAP) - PSUSA/00001320/201709

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Etomidate (NAP) - PSUSA/00001330/201709

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

²¹ Allergen for therapy, oromucosal use only, products authorised via mutually recognition procedure (MRP) and decentralised procedure (DCP) only

Action: For adoption of recommendation to CMDh

6.3.10. Famotidine (NAP) - PSUSA/00001350/201709

Applicant(s): various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Fenoterol²² (NAP) - PSUSA/00001366/201709

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Fluoxetine (NAP) - PSUSA/00001442/201709

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Fluvastatin (NAP) - PSUSA/00001457/201708

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Human von Willebrand factor (NAP) - PSUSA/00001642/201709

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Idebenone²³ (NAP) - PSUSA/00001721/201709

Applicant(s): various

PRAC Lead: John Joseph Borg

²² Respiratory indications only

²³ Non-centrally authorised products only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Latanoprost²⁴ (NAP) - PSUSA/00001834/201710

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Losartan (NAP) - PSUSA/00001912/201709

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Lysine acetylsalicylate (NAP) - PSUSA/00001921/201709

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Metronidazole, neomycin, nystatin (NAP) - PSUSA/00010508/201709

Applicant(s): various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Midazolam²⁵ (NAP) - PSUSA/00002057/201709

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Minocycline (NAP) - PSUSA/00002065/201708

Applicant(s): various

²⁴ Medicinal products with paediatric indication only

²⁵ Except oromucosal solution indicated for the treatment of prolonged, acute, convulsive seizures

PRAC Lead: Dolores Montero Corominas
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.22. Modafinil (NAP) - PSUSA/00010242/201708

Applicant(s): various
PRAC Lead: Martin Huber
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.23. Piperacillin, tazobactam (NAP) - PSUSA/00002425/201709

Applicant(s): various
PRAC Lead: Julie Williams
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.24. Ropivacaine (NAP) - PSUSA/00002662/201709

Applicant(s): various
PRAC Lead: Sabine Straus
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.25. Sodium oxybate²⁶ (NAP) - PSUSA/00010613/201710

Applicant(s): various
PRAC Lead: Ana Sofia Diniz Martins
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.26. Terbinafine (NAP) - PSUSA/00002896/201709

Applicant(s): various
PRAC Lead: Tatiana Magalova
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.27. Treosulfan (NAP) - PSUSA/00009319/201708

Applicant(s): various

²⁶ Intravenous use only

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Tretinoin²⁷ (NAP) - PSUSA/00003016/201708

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Vigabatrin (NAP) - PSUSA/00003112/201709

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/LEG 028

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review of cases of liver injury from all available sources (post marketing cases, clinical trial data and literature) as requested in the conclusions of PSUSA/00000226/201705 adopted at the December 2017 PRAC

Action: For adoption of advice to CHMP

6.4.2. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/LEG 029

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Detailed review on the concomitant use of apixaban and moderate inhibitors of CYP3A4²⁸ and P-glycoprotein in nonvalvular atrial fibrillation (NVAF) patients as requested in the conclusions of PSUSA/00000226/201705 adopted at the December 2017 PRAC

Action: For adoption of advice to CHMP

²⁷ Topical formulations only

²⁸ Cytochrome P450 3A4

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)²⁹

7.1.1. Cidofovir (NAP) - EMEA/H/N/PSP/S/0052.2

Applicant: Emcure Pharma UK Ltd (Cidofovir Emcure Pharma)

PRAC Rapporteur: Julie Williams

Scope: MAH's response to PSP/S/0052.1 [protocol for 'a non-interventional, prospective, exposure (safety outcome) registry study of cidofovir to further elucidate the characteristics of the different patient populations for cidofovir use, gather details of adverse events and patient outcome following treatment in a specified indication'] as per the request for supplementary information (RSI) adopted in July 2017

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

7.1.2. Methylphenidate hydrochloride (NAP) - EMEA/H/N/PSP/S/0064

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

PRAC Rapporteur: To be appointed

Scope: Protocol for a multicentre, observational, prospective PASS to evaluate the safety concerns of long-term cardiovascular and psychiatric risks within the adult attention deficit/hyperactivity disorder (ADHD) population taking Medikinet Retard (methylphenidate hydrochloride) according to normal standard clinical practice

Action: For appointment of a PRAC Rapporteur

7.1.3. Teicoplanin (NAP) - EMEA/H/N/PSA/S/0029

Applicant: Sanofi (Targocid)

PRAC Rapporteur: Valerie Strassmann

Scope: Revised protocol following substantial amendments to a protocol previously agreed by PRAC in June 2015 and amended in May 2017 for a PASS study: a prospective, observational cohort study, evaluating the incidence of nephrotoxicity and other adverse events of interest in patients treated with the higher recommended teicoplanin loading dose (12 mg/kg twice a day), and comparison with external historical comparator data

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)³⁰

7.2.1. Agalsidase beta - FABRAZYME (CAP) - EMEA/H/C/000370/MEA 060.3

Applicant: Genzyme Europe BV

PRAC Rapporteur: Menno van der Elst

²⁹ In accordance with Article 107n of Directive 2001/83/EC

³⁰ 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

Scope: Protocol for a survey to assess the effectiveness of the patient home infusion educational materials in EU countries where the material is implemented [report submission due date: March 2019]

Action: For adoption of advice to CHMP

7.2.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/MEA 010

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of a protocol for an observational study to evaluate the effectiveness of healthcare professional (HCP) educational materials, in particular the HCP brochure aiming at facilitating early recognition and intervention of the following important immune-related risks: pneumonitis, hepatitis, colitis, hypothyroidism, hyperthyroidism, adrenal insufficiency, hypophysitis, type 1 diabetes mellitus (T1DM), neuropathies, meningoencephalitis, pancreatitis, and infusion-related reactions [submission of the final clinical study report (CSR): December 2022]

Action: For adoption of advice to CHMP

7.2.3. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/MEA 002.1

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Doris Stenver

Scope: MAH's response to MEA 002 (listed as a category 3 study in the RMP) [protocol for a non-interventional cohort study to assess characteristics and management of patients with Merkel cell carcinoma in Germany [final report expected in Q1 2024]] as per the request for supplementary information (RSI) adopted in January 2018

Action: For adoption of advice to CHMP

7.2.4. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 003.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 003 [protocol for an observational safety study using an existing database, study I4V-MC-B004: a retrospective cohort 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: 31/03/2031]] as per the request for supplementary information (RSI) adopted in December 2017

Action: For adoption of advice to CHMP

7.2.5. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 004.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 004 [protocol for assessing the effectiveness of the patient

alert card and healthcare professional educational material, study I4V-MC-B010: a rheumatologist survey to assess the effectiveness of the risk minimisation measures (RMM) for Olumiant (baricitinib); and objective 3 of study I4V-MC-B011: a retrospective cohort study to assess the safety of baricitinib compared with other therapies used in the treatment of rheumatoid arthritis in Nordic countries [final report anticipated within 4 months following the end of data] as per the request for supplementary information (RSI) adopted in December 2017

Action: For adoption of advice to CHMP

7.2.6. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 005.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 005 [protocol for an observational post marketing disease registry in EU patients, study I4V-MC-B011: a retrospective cohort study to assess the safety of baricitinib compared with other therapies used in the treatment of rheumatoid arthritis in Nordic countries] as per the request for supplementary information (RSI) adopted in December 2017

Action: For adoption of advice to CHMP

7.2.7. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 008.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 008 [protocol for an observational post marketing disease registry in EU patients, study I4V-MC-B012: a post-marketing safety surveillance of baricitinib in three European registers] as per the request for supplementary information (RSI) adopted in December 2017

Action: For adoption of advice to CHMP

7.2.8. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/MEA 002.1

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: MAH's response to MEA 002 [protocol for a long-term PASS MS 700568-0002: 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)] as per the request for supplementary information (RSI) adopted in January 2018

Action: For adoption of advice to CHMP

7.2.9. Colistimethate sodium - COLOBREATHE (CAP) - EMEA/H/C/001225/MEA 012

Applicant: Teva B.V.

PRAC Rapporteur: Julie Williams

Scope: Progress report on study recruitment and revised protocol for study CLB-MD-08: a cross-sectional study to evaluate the effectiveness of Colobreathe (colistimethate sodium) risk minimisation educational programme among healthcare professionals and patients

Action: For adoption of advice to CHMP

7.2.10. [Infliximab - FLIXABI \(CAP\) - EMEA/H/C/004020/MEA 007.1](#)

Applicant: Samsung Bioepis UK Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 007 [protocol for study SB2-G41-AS; SB2-G42-CD: a prospective observational cohort study in ankylosing spondylitis (AS) and Crohn's disease (CD) for two years to observe safety, efficacy and immunogenicity of Flixabi with active comparator in AS and CD] as per the request for supplementary information (RSI) adopted at the November 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.2.11. [Insulin human - INSUMAN \(CAP\) - EMEA/H/C/000201/MEA 047.5](#)

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 047.4 [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] as per the request for supplementary information (RSI) adopted in January 2018

Action: For adoption of advice to CHMP

7.2.12. [Levetiracetam - KEPBRA \(CAP\) - EMEA/H/C/000277/MEA 086.3](#)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to MEA 086.1 [protocol for PASS EPD172 comparing the incidence of renal failure in patients with epilepsy exposed to levetiracetam or other antiepileptic drugs (AED)] as per the request for supplementary information (RSI) adopted in December 2017

Action: For adoption of advice to CHMP

7.2.13. [Loxapine - ADASUVE \(CAP\) - EMEA/H/C/002400/MEA 001.4](#)

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Sabine Straus

Scope: MAH's response to MEA 001.3 [revised protocols for: 1) study AMDC-204-401 (PASS): a post-authorisation observational study to evaluate the safety of Adasuve

(loxapine for inhalation) in agitated persons in routine clinical care and study; 2) study 204-403 (drug utilisation study (DUS)): a multinational retrospective medical record to evaluate utilisation patterns of Adasuve (loxapine for inhalation) in agitated persons in routine clinical care] as per the request for supplementary information (RSI) adopted in December 2017

Action: For adoption of advice to CHMP

7.2.14. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/MEA 002

Applicant: Tesaro UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Protocol for study 3000-04-001: a non-interventional PASS to evaluate the risks of myelodysplastic syndrome/acute myeloid leukaemia and secondary primary malignancies in adult patients with relapsed ovarian, fallopian tube, or primary peritoneal cancer receiving maintenance treatment with Zejula (niraparib)

Action: For adoption of advice to CHMP

7.2.15. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) – MOSQUIRIX (Art 58³¹) - EMEA/H/W/002300/MEA 002.1

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Scientific Opinion Holder (SOH)'s response to MEA 002 [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)] as per the request for supplementary information (RSI) adopted in January 2018

Action: For adoption of advice to CHMP

7.2.16. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) – MOSQUIRIX (Art 58³²) - EMEA/H/W/002300/MEA 003.1

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Scientific Opinion Holder (SOH)'s response to MEA 003 [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] as per the request for supplementary information (RSI) adopted in January 2018

Action: For adoption of advice to CHMP

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)

³² 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)

7.2.17. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 002.1

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: MAH's response to MEA 002 [protocol for study A3921133 (RMP category 3): a phase 3B/4 randomised safety endpoint study of 2 doses of tofacitinib in comparison to a tumour necrosis factor (TNF) inhibitor in subjects with rheumatoid arthritis (RA) [final report due date: by 31 December 2020] as per the request for supplementary information (RSI) adopted in December 2017

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)³³

7.3.1. Magnesium sulfate heptahydrate, sodium sulfate anhydrous, potassium sulfate (NAP) - EMEA/H/N/PSR/S/0016

Applicant(s): Ipsen Pharma (Eziclen, Izinova)

PRAC Rapporteur: Caroline Laborde

Scope: Results for a multicentre, European, observational, drug utilisation study (DUS) of Eziclen/Izinova (BLI800) (magnesium sulfate heptahydrate/sodium sulfate anhydrous/potassium sulfate) as a bowel cleansing preparation to document the misuse of BLI800, defined as non-compliance in terms of insufficient liquid intake, during the post approval period in the real life setting; and to describe the safety profile of BLI800 in routine clinical practice, overall and in case of misuse defined as non-compliance in terms of insufficient liquid intake, and identify any immediate/acute adverse events associated with the use of BLI800 in special populations (i.e. the elderly and patients at risk for electrolyte shifts)

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)³⁴

7.4.1. Asenapine - SYCREST (CAP) - EMEA/H/C/001177/II/0031/G

Applicant: N.V. Organon

PRAC Rapporteur: Julie Williams

Scope: Grouped variations consisting of the submission of final reports for the following studies (listed as category 3 studies in the RMP), namely: 1) study P08307 (EP04026.001): an observational PASS of Sycrest (asenapine) among patients aged 18 and older diagnosed with bipolar disorder [EU PAS register number: EUPAS17631]; 2) study P08308 (EP04026.003): an observational drug utilisation study (DUS) of Sycrest (asenapine) in the United Kingdom [EU PAS register number: EUPAS17681]; 3) study P08309 (EP04026.002): an observational post-authorisation modified prescription-event monitoring safety study to monitor the safety and utilisation of Sycrest (asenapine) In the primary care setting in

³³ In accordance with Article 107p-q of Directive 2001/83/EC

³⁴ 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

England [EU PAS Register: EUPAS3603]; 4) study P08310 (EP04026.004): an observational post-authorisation safety specialist cohort event monitoring study (SCEM) to monitor the safety and utilisation of Sycrest (asenapine) in the mental health care setting in England and Wales [EU PAS Register: EUPAS3136]. No changes to the product information (PI) are proposed. The RMP (version 5.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Buprenorphine, naloxone - SUBOXONE (CAP) - EMEA/H/C/000697/II/0037

Applicant: Indivior UK Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report for study PEUS005: 'a mortality study in the UK using the Health Improvement Network Database (THIN)' in order to estimate the all-cause mortality amongst patients exposed to Suboxone (buprenorphine/naloxone) in comparison to buprenorphine and methadone. The RMP (version 13.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/WS1270/0216; LIFMIOR (CAP) - EMEA/H/C/004167/WS1270/0013

Applicant: Pfizer Limited

PRAC Rapporteur: Patrick Batty

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

Action: For adoption of PRAC Assessment Report

7.4.4. Mannitol - BRONCHITOL (CAP) - EMEA/H/C/001252/II/0031, Orphan

Applicant: Pharmaxis Pharmaceuticals Limited

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report of a survey on healthcare professionals (listed as a category 3 study in the RMP): a final survey aimed at measuring the effectiveness of the educational materials at 6 month post-launch and 6 month post-redistribution of the revised healthcare professional leaflet. The RMP (version 7.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. Sevelamer carbonate - RENVELA (CAP) - EMEA/H/C/000993/II/0043

Applicant: Genzyme Europe BV

PRAC Rapporteur: Laurence de Fays

Scope: Submission of the final report from study SEVELC08371: a historical cohort study of adult patients with severe chronic kidney disease (CKD) assessing the risk of bladder cancer by sevelamer exposure

Action: For adoption of PRAC Assessment Report

7.4.6. [Emtricitabine, tenofovir disoproxil - TRUVADA \(CAP\) - EMEA/H/C/000594/WS1326/0145;](#)
[Tenofovir disoproxil - VIREAD \(CAP\) - EMEA/H/C/000419/WS1326/0184](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Caroline Laborde

Scope: Submission of the final report from study GS-EU-104-0433 (listed as a category 3 study in the RMP): an observational, drug utilisation study (DUS) of Viread (emtricitabine/tenofovir disoproxil) in children and adolescents with human immunodeficiency virus-1 (HIV-1) infection, in fulfilment of a post-authorisation measure (PAM) for Viread (emtricitabine/tenofovir disoproxil) (MEA 46) and Truvada (tenofovir disoproxil) (MEA 276)

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. [Abatacept - ORENCIA \(CAP\) - EMEA/H/C/000701/MEA 048.6](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Annual update report on recruitment for study IM101240: an observational registry of abatacept in patients with juvenile idiopathic arthritis (JIA registry) to explore the long-term safety of abatacept treatment for JIA in routine clinical practice (final registry report due date by 2029)

Action: For adoption of advice to CHMP

7.5.2. [Adalimumab - HUMIRA \(CAP\) - EMEA/H/C/000481/MEA 065.8](#)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Ninth interim report for study P10-023, a psoriasis patient registry: a 10-year, post-marketing observational study to assess the long term safety of Humira (adalimumab) in adult patients with chronic plaque psoriasis (PS)) (due date: final registry report planned in February 2023)

Action: For adoption of advice to CHMP

7.5.3. [Alemtuzumab - LEMTRADA \(CAP\) - EMEA/H/C/003718/MEA 007.5](#)

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Anette Kirstine Stark

Scope: Third annual report for study OBS13434: a prospective, multicentre, observational PASS to evaluate the long term safety profile of Lemtrada (alemtuzumab) treatment in patients with relapsing forms of multiple sclerosis (MS) and to determine the incidence of adverse events of special interest (AESIs)

Action: For adoption of advice to CHMP

7.5.4. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.12

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fifth annual interim report for study BEL116543/HGS1006-C1124: a long-term controlled safety registry evaluating the incidence of all-cause mortality and adverse events of special interest in patients with systemic lupus erythematosus followed for a minimum of 5 years

Action: For adoption of advice to CHMP

7.5.5. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/MEA 001.3

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Third annual interim report for EuroSIDA PASS study 201177 (listed as a category 3 study in the RMP): a prospective observational cohort study in patients receiving dolutegravir 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)

Action: For adoption of advice to CHMP

7.5.6. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/MEA 007.3

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Third annual interim report for EuroSIDA PASS study 201177 (listed as a category 3 study in the RMP): a prospective observational cohort study in patients receiving dolutegravir 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)

Action: For adoption of advice to CHMP

7.5.7. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 007.3

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 007.2 [third annual report from a pregnancy research initiative to study the exposure to golimumab during pregnancy in patients with rheumatoid

arthritis, psoriatic arthritis, and ankylosing spondylitis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers (CNT0148ART4001) and US health assurance claim database (CNT0148ART4002)] as per the request for supplementary information adopted at the December 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.5.8. Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/MEA 041.1

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Second annual interim study report of the Insuman implantable registry HUBIN-C-06380: a European observational cohort of patients with type 1 diabetes treated via intraperitoneal route with Insuman implantable 400 IU/mL in Medtronic MiniMed implantable pump

Action: For adoption of advice to CHMP

7.5.9. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/MEA 028.6

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Sixth interim report of a PASS study (listed as a category 3 study in the RMP): a post-approval safety surveillance for monthly lot-specific adverse event review and analysis to evaluate any potential change in the frequency of hypersensitivity and immunogenicity events with the altered manufacturing process of Humalog and Liprolog (insulin lispro). This sixth report covers the batches released to the market between 15 October 2013 and 31 January 2018

Action: For adoption of advice to CHMP

7.5.10. Insulin lispro - LIPROLOG (CAP) - EMEA/H/C/000393/MEA 021.6

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Sixth interim report of a PASS study (listed as a category 3 study in the RMP): a post-approval safety surveillance for monthly lot-specific adverse event review and analysis to evaluate any potential change in the frequency of hypersensitivity and immunogenicity events with the altered manufacturing process of Humalog and Liprolog (insulin lispro). This sixth report covers the batches released to the market between 15 October 2013 and 31 January 2018

Action: For adoption of advice to CHMP

7.5.11. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 005.2

Applicant: Teva Pharmaceuticals Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Results of a feasibility assessment conducted in US healthcare databases as per the

agreed protocol (final version dated 25 May 2017) for study C38072-AS-50027: a long-term non-interventional cohort study comparing the risk of malignancy in severe asthma patients treated with reslizumab and patients not treated with reslizumab using secondary administrative healthcare data (listed as category 3 in the RMP]

Action: For adoption of advice to CHMP

7.5.12. Roflumilast - DAXAS (CAP) - EMEA/H/C/001179/ANX 002.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to ANX 002.4 [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 (Annex II-D condition) [final clinical study report (CSR) expected in March 2031]] as per the request for supplementary information (RSI) adopted in January 2018

Action: For adoption of advice to CHMP

7.5.13. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/MEA 273.3

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Caroline Laborde

Scope: Interim report for PASS study GS-EU-174-1846: a multicentre, non-interventional, retrospective cohort study of patients with chronic hepatitis B (CHB) and with moderate to severe renal impairment treated with Viread (tenofovir disoproxil)

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Canakinumab - ILARIS (CAP) - EMEA/H/C/001109/MEA 037.4

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Amendment to the statistical analysis plan (SAP) for study CACZ885G2403: a non-interventional study collecting safety data from systemic juvenile idiopathic arthritis (SJIA) patients enrolled in the Childhood Arthritis & Rheumatology Research Alliance (CARRA) disease registry who initiate treatment with canakinumab or comparator, with no change in the study protocol

Action: For adoption of advice to CHMP

7.6.2. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 012

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Statistical analysis plan (SAP) (edition 1.0) for the meta-analysis for incidence of

amputation and assessment of potential relevant preceding adverse events of interest for the following studies, namely: 1) study D1693C00001 (DECLARE): a multicentre, randomized, double-blind, placebo-controlled trial to evaluate the effect of dapagliflozin 10 mg once daily on the incidence of cardiovascular death, myocardial infarction or ischemic stroke in patients with type 2 diabetes mellitus (T2DM); 2) study D1690C00018: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled, phase 3 study with a 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg once daily in patients with T2DM, cardiovascular disease and hypertension who exhibit inadequate glycaemic control on usual care; 3) study D1690C00019: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled phase 3 study with an 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg Once daily in patients with T2DM and cardiovascular disease, who exhibit inadequate glycaemic control on usual care, in line with the conclusions of the procedure under Article 20 of Regulation (EC) No 726/2004 on sodium-glucose co-transporter-2 (SGLT2) inhibitors completed in 2017 (A-20/1442/C/4161)

Action: For adoption of advice to CHMP

7.6.3. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/MEA 024

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Statistical analysis plan (SAP) (edition 1.0) for the meta-analysis for incidence of amputation and assessment of potential relevant preceding adverse events of interest for the following studies, namely: 1) study D1693C00001 (DECLARE): a multicentre, randomized, double-blind, placebo-controlled trial to evaluate the effect of dapagliflozin 10 mg once daily on the incidence of cardiovascular death, myocardial infarction or ischemic stroke in patients with type 2 diabetes mellitus (T2DM); 2) study D1690C00018: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled, phase 3 study with a 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg once daily in patients with T2DM, cardiovascular disease and hypertension who exhibit inadequate glycaemic control on usual care; 3) study D1690C00019: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled phase 3 study with an 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg Once daily in patients with T2DM and cardiovascular disease, who exhibit inadequate glycaemic control on usual care, in line with the conclusions of the procedure under Article 20 of Regulation (EC) No 726/2004 on sodium-glucose co-transporter-2 (SGLT2) inhibitors completed in 2017 (A-20/1442/C/4161)

Action: For adoption of advice to CHMP

7.6.4. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/MEA 011

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Statistical analysis plan (SAP) (edition 1.0) for the meta-analysis for incidence of amputation and assessment of potential relevant preceding adverse events of interest for the following studies, namely: 1) study D1693C00001 (DECLARE): a multicentre, randomized, double-blind, placebo-controlled trial to evaluate the effect of dapagliflozin 10

mg once daily on the incidence of cardiovascular death, myocardial infarction or ischemic stroke in patients with type 2 diabetes mellitus (T2DM); 2) study D1690C00018: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled, phase 3 study with a 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg once daily in patients with T2DM, cardiovascular disease and hypertension who exhibit inadequate glycaemic control on usual care; 3) study D1690C00019: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled phase 3 study with an 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg Once daily in patients with T2DM and cardiovascular disease, who exhibit inadequate glycaemic control on usual care, in line with the conclusions of the procedure under Article 20 of Regulation (EC) No 726/2004 on sodium-glucose co-transporter-2 (SGLT2) inhibitors completed in 2017 (A-20/1442/C/4161)

Action: For adoption of advice to CHMP

7.6.5. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 014

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Statistical analysis plan (SAP) (edition 1.0) for the meta-analysis for incidence of amputation and assessment of potential relevant preceding adverse events of interest for the following studies, namely: 1) study D1693C00001 (DECLARE): a multicentre, randomized, double-blind, placebo-controlled trial to evaluate the effect of dapagliflozin 10 mg once daily on the incidence of cardiovascular death, myocardial infarction or ischemic stroke in patients with type 2 diabetes mellitus (T2DM); 2) study D1690C00018: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled, phase 3 study with a 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg once daily in patients with T2DM, cardiovascular disease and hypertension who exhibit inadequate glycaemic control on usual care; 3) study D1690C00019: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled phase 3 study with an 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg Once daily in patients with T2DM and cardiovascular disease, who exhibit inadequate glycaemic control on usual care, in line with the conclusions of the procedure under Article 20 of Regulation (EC) No 726/2004 on sodium-glucose co-transporter-2 (SGLT2) inhibitors completed in 2017 (A-20/1442/C/4161)

Action: For adoption of advice to CHMP

7.6.6. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/REC 030.5

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Sixth report on the monthly analysis of relevant drug event combination (DEC) for events reported with current-process Humalog (insulin lispro) compared with new-process Humalog (covering the period from 15 October 2013 to 31 January 2018) (from WS/0679)

Action: For adoption of advice to CHMP

7.6.7. Insulin lispro - LIPROLOG (CAP) - EMEA/H/C/000393/REC 023.5

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Sixth report on the monthly analysis of relevant drug event combination (DEC) for events reported with current-process Liprolog (insulin lispro) compared with new-process Liprolog (covering the period from 15 October 2013 to 31 January 2018) (from WS/0679)

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. Histamine dihydrochloride - CEPLENE (CAP) - EMEA/H/C/000796/S/0035 (without RMP)

Applicant: Noventia Pharma Srl

PRAC Rapporteur: Almath Spooner

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/S/0044 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/R/0003 (without RMP)

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Doris Stenver

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/R/0041 (without RMP)

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/R/0087 (without RMP)

Applicant: Noden Pharma DAC

PRAC Rapporteur: Carmela Macchiarulo

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (Δ LNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - ZALMOXIS (CAP) - EMEA/H/C/002801/R/0010 (without RMP)

Applicant: MolMed SpA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Aripiprazole - ABILIFY MAINTENA (CAP) - EMEA/H/C/002755/R/0025 (with RMP)

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. [Canagliflozin - INVOKANA \(CAP\) - EMEA/H/C/002649/R/0037 \(without RMP\)](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. [Cobicistat - TYBOST \(CAP\) - EMEA/H/C/002572/R/0041 \(with RMP\)](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. [Etravirine - INTELENCE \(CAP\) - EMEA/H/C/000900/R/0052 \(with RMP\)](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Caroline Laborde

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. [Fluticasone furoate, vilanterol - RELVAR ELLIPTA \(CAP\) - EMEA/H/C/002673/R/0037 \(without RMP\)](#)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. [Fluticasone furoate, vilanterol - REVINTY ELLIPTA \(CAP\) - EMEA/H/C/002745/R/0033 \(without RMP\)](#)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. [Histamine dihydrochloride - CEPLENE \(CAP\) - EMEA/H/C/000796/R/0036 \(with RMP\)](#)

Applicant: Noventia Pharma Srl

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Human fibrinogen, human thrombin - EVICEL (CAP) - EMEA/H/C/000898/R/0054 (without RMP)

Applicant: Omrix Biopharmaceuticals N. V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Lidocaine, prilocaine - FORTACIN (CAP) - EMEA/H/C/002693/R/0023 (with RMP)

Applicant: Recordati Ireland Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Macitentan - OPSUMIT (CAP) - EMEA/H/C/002697/R/0027 (with RMP)

Applicant: Actelion Registration Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Mercaptamine - PROCYSBI (CAP) - EMEA/H/C/002465/R/0019 (with RMP)

Applicant: Chiesi Orphan B.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.14. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/R/0039 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.15. Turoctocog alfa - NOVOEIGHT (CAP) - EMEA/H/C/002719/R/0025 (with RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Dolutegravir – TIVICAY (CAP) - EMEA/H/C/002753/II/0034 Dolutegravir, abacavir, lamivudine – TRIUMEQ (CAP) - EMEA/H/C/002754/II/0053

Applicant(s): ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams; PRAC representative of the CHMP Rapporteur's delegation: Qun-Ying Yue

Scope: Consultation on type II variations to update section 4.8 of the SmPC to add the new adverse drug reactions (ADRs) 'acute hepatic failure' and 'weight increased' based on post-marketing and clinical trial data. The package leaflet is updated accordingly

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

11.2.1. Tretinoin³⁵ (NAP)

Applicant: Cheplapharm Arzneimittel GmbH (Vesanoid)

PRAC Lead: Martin Huber

Scope: Consultation on the need for updated communication materials for tretinoin-containing products following the completion of the referral procedure on retinoids under Article 31 of Directive 2001/83/EC in March 2018 (EMA/H/A-31/1446)

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

None

12.4. Cooperation within the EU regulatory network

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

Action: For discussion

12.4.2. PRAC strategic review and learning meeting (SRLM) – results from the questionnaire on adverse drug reactions (ADR) to vaccines and pharmacovigilance newsletter

PRAC lead: Eva Jirsová

Action: For discussion

³⁵ For oral use, in oncology indication(s) only

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q1 2018 and predictions

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: 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. Guideline on Good Pharmacovigilance Practices (GVP) – Product- or population-specific considerations IV: ‘Paediatric pharmacovigilance’

Action: For adoption

12.20.2. Initial marketing authorisation applications (MAA) and Generics MAA – review of rapporteur assessment report templates – roll out Spring 2018

Action: For adoption

13. Any other business

Next meeting on: 11-14 June 2018

14. Explanatory notes

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

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures (Items 2 and 3 of the PRAC agenda)

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

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

Signals assessment and prioritisation (Item 4 of the PRAC agenda)

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

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

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

Risk Management Plans (RMPs) (Item 5 of the PRAC agenda)

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

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

Assessment of Periodic Safety Update Reports (PSURs) (Item 6 of the PRAC agenda)

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

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

Post-authorisation Safety Studies (PASS) (Item 7 of the PRAC agenda)

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

Product related pharmacovigilance inspections (Item 9 of the PRAC agenda)

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

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