6 June 2017
EMA/PRAC/355498/2017

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 6-9 June 2017

Chair: June Raine – Vice-Chair: Almath Spooner

6 June 2017, 13:00 – 19:30, room 3/A

7 June 2017, 08:30 – 19:30, room 3/A

8 June 2017, 08:30 – 19:30, room 3/A

9 June 2017, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

22 June 2017, 09:00-12:00, room 7/B, via adobe connect

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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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 6-9 June 2017. See June 2017 PRAC minutes (to be published post July 2017 PRAC meeting).

1.2. Agenda of the meeting on 6-9 June 2017

Action: For adoption

1.3. Minutes of the previous meeting on 2-5 May 2017

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

2.4. Planned public hearings

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. 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)

Applicant: 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 information

3.2.2. Lactose of bovine origin-containing medicinal products[1]: methylprednisolone (NAP) - EMEA/H/A-31/1449

Applicant: Pfizer Croatia d.o.o. (Solu-Medrol), various

PRAC Rapporteur: Jan Neuhauser; PRAC Co-rapporteur: Nikica Mirošević Skvrce

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

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

3.2.3. Valproate and related substances: sodium valproate, valproic acid, valproate semisodium, valpromide (NAP)

Applicant: Sanofi-Aventis, various

PRAC Rapporteur: Sabine Straus; PRAC Co-rapporteur: Jean-Michel Dogné

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

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

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

3.4.1. Gadolinium-containing contrast agents (GdCA): gadobenic acid (NAP); gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid

[1] For intravenous (IV) or intramuscular (IM) use indicated for the treatment of acute allergic reactions only
[2] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

(NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoversetamide – OPTIMARK (CAP); gadoxetic acid (NAP) - EMEA/H/A-31/1437

Applicant(s): Mallinckrodt Deutschland GmbH (Optimark); various

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Valerie Strassmann

Scope: Re-examination procedure under Article 32 of Directive 2001/83/EC of the review of the benefit-risk balance of GdCA following notification by the European Commission of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For discussion

3.5. Others

3.5.1. Human coagulation (plasma -derived) factor VIII: human coagulation factor VIII (antihemophilic factor A) (NAP); human coagulation factor VIII (inhibitor bypassing fraction) (NAP); human coagulation factor VIII, human von Willebrand factor - VONCENTO (CAP)
Recombinant factor VIII: antihemophilic factor (recombinant) (NAP); efmoroctocog alfa – ELOCTA (CAP); moroctocog alfa – REFACTO AF (CAP) octocog alfa – ADVATE (CAP), HELIXATE NEXGEN (CAP), IBLIAS (CAP), KOGENATE (CAP), KOVALTRY (CAP); turoctocog alfa – NOVOEIGHT (CAP); simoctocog alfa – NUWIQ (CAP); susoctocog alfa – OBIZUR (CAP) - EMEA/H/A-31/1448

Applicant(s): Baxter AG (Advate), Bayer Pharma AG (Helixate Nexgen, Iblias, Kogenate, Kovaltry), CSL Behring GmbH (Voncento), Novo Nordisk A/S (NovoEight), Octapharma AB (Nuwiq), Pfizer Limited (Refacto AF), Swedish Orphan Biovitrum AB (publ) (Elocta), Baxalta Innovations GmbH (Obizur), various

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

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

Scope: Request for re-examination under Article 32 of Directive 2001/83/EC of the review of the benefit-risk balance following notification by the European Commission of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For discussion

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Amitriptyline (NAP)

Applicant(s): various

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

PRAC Rapporteur: To be appointed

Scope: Signal of risk of drug induced liver injury (DILI) and hepatocellular injury

Action: For adoption of PRAC recommendation

EPITT 18890 – New signal

Lead Member State(s): EL

4.1.2. Ledipasvir, sofosbuvir – HARVONI (CAP)

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Signal of blood cholesterol, low density lipoprotein increased

Action: For adoption of PRAC recommendation

EPITT 18903 – New signal

Lead Member State(s): PT

4.1.3. mTOR[4] inhibitors: everolimus – AFINITOR (CAP), VOTUBIA (CAP), NAP; sirolimus – RAPAMUNE (CAP); temsirolimus – TORISEL (CAP)

Applicant(s): Novartis Europharm Ltd (Afinitor, Votubia), Pfizer Limited (Rapamune, Torisel), various

PRAC Rapporteur: To be appointed

Scope: Signal of optic neuropathy and papilloedema

Action: For adoption of PRAC recommendation

EPITT 18901 – New signal

Lead Member State(s): SE, DE

4.1.4. Telmisartan – KINZALKOMO (CAP), MICARDIS (CA), PRITOR (CAP), TELMISARTAN ACTAVIS (CAP), TELMISARTAN TEVA (CAP), TELMISARTAN TEVA PHARMA (CAP), TOLURA (CAP); telmisartan, hydrochlorothiazide - ACTELSAR HCT (CAP), KINZALKOMB (CAP), MICARDIS PLUS (CAP), PRITOR PLUS (CAP), TOLUCOMBI (CAP); telmisartan, amlodipine – TWYNSTA (CAP); NAP

Applicant(s): Bayer Pharma AG (Kinzalmono, Kinzalkomb, Pritor, Pritor Plus), Boehringer Ingelheim International GmbH (Micardis, Micardis Plus, Twynsta), Actavis Group PTC ehf (Telmisartan Actavis, Actelsar HCT), Teva B.V.(Telmisartan Teva, Telmisartan Teva Pharma), KRKA, d.d., Novo mesto (Tolura, Tolucombi); various

PRAC Rapporteur: To be appointed

Scope: Signal of risk of psoriasis or exacerbation of psoriasis

Action: For adoption of PRAC recommendation

EPITT 18882 – New signal

[4] Mechanistic target of rapamycin

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

4.2. New signals detected from other sources

4.2.1. Dasatinib – SPRYCEL (CAP); warfarin (NAP)

Applicant(s): Bristol-Myers Squibb Pharma EEIG (Sprycel); various

PRAC Rapporteur: To be appointed

Scope: Signal of serious adverse drug reactions (ADRs) including bleeding events following potential drug interaction between dasatinib and warfarin

Action: For adoption of PRAC recommendation

EPITT 18894 – New signal

Lead Member State(s): DK

4.2.2. Phenprocoumon (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal related to risk of birth defects and foetal loss following first trimester exposure as a function of the time of withdrawal

Action: For adoption of PRAC recommendation

EPITT 18902 – New signal

Lead Member State(s): DE

4.2.3. Prednisolone (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of induced scleroderma renal crisis

Action: For adoption of PRAC recommendation

EPITT 18888 – New signal

Lead Member State(s): DK

4.3. Signals follow-up and prioritisation

4.3.1. Dabigatran – PRADAXA (CAP) – EMEA/H/C/000829/SDA/047; lovastatin (NAP); simvastatin (NAP)

Applicant(s): Boehringer Ingelheim International GmbH (Pradaxa), various

PRAC Rapporteur: Torbjorn Callreus

Scope: Signal of major haemorrhage following dabigatran interaction with simvastatin or lovastatin

Action: For adoption of PRAC recommendation

EPITT 18819 – Follow-up to February 2017

4.3.2. Dabrafenib – TAFINLAR (CAP) - EMEA/H/C/002604/SDA/012; trametinib – MEKINIST (CAP) - EMEA/H/C/002643/SDA/009

Applicant(s): Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of sepsis

Action: For adoption of PRAC recommendation

EPITT 18779 – Follow-up to December 2016

4.3.3. Docetaxel – TAXOTERE (CAP), DOCETAXEL ACCORD (CAP), TAXESPIRA (CAP)

Applicant(s): Aventis Pharma S.A. (Taxotere), Accord Healthcare Ltd (Docetaxel Accord), Hospira UK Limited (Taxespira), various

PRAC Rapporteur: Claire Ferard

Scope: Signal of unexpected seriousness of reported adverse drug reactions (ADRs) with docetaxel in particular neutropenic enterocolitis and suspicion of an increase in ADR reporting rate in France with docetaxel-containing products

Action: For adoption of PRAC recommendation

EPITT 12059 – Follow up to April 2017

4.3.4. Gabapentin (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal of respiratory depression without concomitant opioid use

Action: For adoption of PRAC recommendation

EPITT 18814 - Follow-up to January 2017

4.3.5. Intravenous (IV) fluids containing electrolytes and/or carbohydrates (NAP)

Applicant(s): various

PRAC Rapporteur: Doris Stenver

Scope: Signal of hyponatremia

Action: For adoption of PRAC recommendation

EPITT 18631 – Follow-up to April 2017

4.3.6. Levonorgestrel[5] (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal of anxiety, panic attacks, mood changes, sleep disorders and restlessness

Action: For adoption of PRAC recommendation

EPITT 18849 – Follow-up to February 2017

4.3.7. Tick-borne encephalitis vaccine[6] (NAP)

Applicant(s): various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of potential vaccination failure in children

Action: For adoption of PRAC recommendation

EPITT 18825 – Follow-up to February 2017

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Avelumab - EMEA/H/C/004338, Orphan

Applicant: Merck Serono Europe Limited

Scope: Treatment of Merkel cell carcinoma (MCC)

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

5.1.2. Entecavir - EMEA/H/C/004458

Scope: Treatment of chronic hepatitis B virus (HBV) infection

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

5.1.3. Glibenclamide - EMEA/H/C/004379, Orphan

Applicant: Ammtek

Scope: Treatment of neonatal diabetes

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

[5] Intrauterine device (IUD)
[6] Inactivated

5.1.4. Imatinib - EMEA/H/C/004748

Scope: Treatment of newly diagnosed and chronic Philadelphia chromosome (BCR-Abl) positive (Ph+) chronic myeloid leukaemia (CML), gastrointestinal stromal tumours (GIST), unresectable dermatofibrosarcoma protuberans (DFSP) and recurrent and/or metastatic DFSP

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

5.1.5. Lacosamide - EMEA/H/C/004443

Scope: Treatment of epilepsy

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

5.1.6. Miglustat - EMEA/H/C/004366

Scope: Treatment of Gaucher disease

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

5.1.7. Niraparib - EMEA/H/C/004249, Orphan

Applicant: Tesaro UK Limited

Scope: Treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer

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

5.1.8. Sirukumab - EMEA/H/C/004165

Scope: Treatment of rheumatoid arthritis (RA)

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

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

5.2.1. Albiglutide - EPERZAN (CAP) - EMEA/H/C/002735/II/0029/G

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: Grouped variation to: 1) update the RMP to amend the category 3 study 201805: an observational study of the risk of common malignant neoplasms and malignant neoplasms of special interest (thyroid and pancreatic cancer) in subjects prescribed albiglutide compared to those prescribed other antidiabetic agents, in order to use a different database to study the risk of neoplasms in association with albiglutide exposure; 2) update the RMP to add a new category 3 study as an additional pharmacovigilance activity study 207351: an observational study to assess maternal and foetal outcomes following exposure to albiglutide during pregnancy

Action: For adoption of PRAC Assessment Report

5.2.2. Bevacizumab - AVASTIN (CAP) - EMEA/H/C/000582/II/0095

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Update of the RMP (version 28.0) in order to remove the post-authorisation measure (PAM) relating to the submission of an extension protocol to obtain additional long-term follow-up (LTFU) information from the paediatric population after patients complete a minimum of 5.5 year follow-up period as defined in the protocol of study BO20924 (BERNIE): an open-label, multicentre, randomized study of the safety and effect on event-free survival of bevacizumab in combination with standard chemotherapy in childhood and adolescent patients with metastatic rhabdomyosarcoma and non-rhabdomyosarcoma soft tissue sarcoma, as well as to amend the submission date of its final report (addendum clinical study report (CSR))

Action: For adoption of PRAC Assessment Report

5.2.3. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0065

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 18) to update the 'important potential risk: hypercalcemia following treatment discontinuation in patients with growing skeletons' to 'important potential risk: hypercalcemia following treatment discontinuation in patients with growing skeletons and the adult population'. The RMP is updated based on the MAH's updated safety assessment conducted in 2016. The MAH also took the opportunity to request the removal of the important potential risk of fracture healing complications as recommended in April 2016 by PRAC in procedure EMEA/H/C/PSUSA/00000954/201509. Furthermore, addition of study 20090601: a post-marketing active safety surveillance programme for soliciting adverse events of special interest in the United States as a category 4 study pharmacovigilance activity

Action: For adoption of PRAC Assessment Report

5.2.4. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0051

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 23) to update the 'important potential risk: hypercalcemia following treatment discontinuation in patients with growing skeletons' with the new important potential risk: hypercalcemia following treatment discontinuation in patients other than those with growing skeletons'. The MAH also took the opportunity to include minor changes for correction and/or to add clarification

Action: For adoption of PRAC Assessment Report

5.2.5. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0054

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 25) in order to reflect that cataract is no longer considered as a potential risk associated with denosumab therapy, following the recent completion of study 20080560 (a phase 3, randomized, double-blind, placebo-controlled study to evaluate new or worsening lens opacifications in subjects with non-metastatic prostate cancer receiving denosumab for bone loss due to androgen deprivation therapy) where results showed no difference between the risk of developing cataracts in the denosumab and placebo groups

Action: For adoption of PRAC Assessment Report

5.2.6. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58) - EMEA/H/W/002300/II/0020

Applicant: GSK Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of the RMP (version 3.0) in order to 1) add cerebral malaria as an important potential risk, 2) add mortality by gender as missing information, 3) add the WHO[7] pilot implementation programme as a category 3 study, 4) change the study dates for studies malaria-073 (200596, phase IIIb randomized, open, controlled study to evaluate the immunogenicity and safety of Mosquirix, when administered as primary vaccination at 6, 7.5 and 9 months of age with or without coadministration of measles and rubella and yellow fever vaccines to children living in sub-Saharan, Africa), EPI-MAL-002 (115055, an observational cohort study to estimate the incidence of adverse event of special interest (AESI), of meningitis and of other adverse events (AE) leading to hospitalisation or death, in children, prior to implementation of Mosquirix), EPI-MAL-003 (115056, a prospective surveillance study to evaluate the safety, the effectiveness and the impact of Mosquirix in infants and young children in sub-Saharan Africa), EPI-MAL-005 (116682, an epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post-Mosquirix introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit-risk in children in sub-Saharan Africa), EPI-MAL-010 (205071, a longitudinal, cross-sectional ancillary study of the EPI-MAL-005 study to evaluate the genetic diversity in circumsporozoite sequences before and after the implementation of Mosquirix in malaria-positive subjects ranging from 6 months to less than 5 years of age), 5) amend the protocol of study EPI-MAL-002, 6) update the draft protocol of study EPI-MAL-003, 7) provide a new draft of the protocol of study EPI-MAL-010, 8) provide a new protocol for the pilot implementation programme

Action: For adoption of PRAC Assessment Report

5.2.7. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/II/0038, Orphan

Applicant: Incyte Biosciences UK Ltd

PRAC Rapporteur: Patrick Batty

Scope: Update of the RMP (version 17) in order to provide the statistical analysis plan (SAP) for study AP24534-14-401 (a post-marketing observational cohort study to evaluate the incidence of and risk factors for vascular occlusive events associated with Iclusig in routine

[7] World Health Organization

clinical practice in the United States (US)), as per the PRAC request made in the framework of MEA 015

Action: For adoption of PRAC Assessment Report

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

5.3.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/II/0105

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Extension of indication to include the treatment of psoriatic arthritis in adults. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP (version 21) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

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

5.3.2. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/II/0001

Applicant: Roche Registration Limited

PRAC Rapporteur: Patrick Batty

Scope: Extension of indication to first line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC). As a consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 2.0) are updated accordingly

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

5.3.3. Aliskiren - RASILEZ (CAP) - EMEA/H/C/000780/WS1026/0110; aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/WS1026/0080

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of section 5.1 of the SmPC in order to reflect the results of study SPP100F2301 (ATMOSPHERE): a multicentre, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (New York Heart Association (NYHA) Class II-IV). The RMP (version 13) is updated accordingly

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

5.3.4. Atazanavir sulfate - REYATAZ (CAP) - EMEA/H/C/000494/II/0111

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Caroline Laborde

Scope: Update of sections 4.4 and 4.8 of the SmPC to add a warning on chronic kidney disease (CKD) observed in human immunodeficiency virus (HIV) infected patients during treatment with atazanavir (with or without ritonavir). This update is based on a review of the MAH safety database, a cohort study of patients with laboratory values from a large US administrative claims database and a review of published scientific literature. The Package Leaflet and the RMP (version 12.0) are updated accordingly

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

5.3.5. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/X/0046/G

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped application consisting of: 1) line extension to introduce a new pharmaceutical form (solution for injection), a new strength (200 mg) and a new route of administration (subcutaneous use); 2) update of sections 4.2, 4.8, 5.1 and 5.2 for the authorised presentations (Benlysta powder for concentrate for solution for infusion) as a consequence of the data package submitted to support the new proposed solution for injection subcutaneous. The RMP (version 21) is updated accordingly

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

5.3.6. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0011, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and amend the safety information. The Labelling and the RMP (version 4.0) are updated accordingly

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

5.3.7. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0045, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Update of section 5.1 of the SmPC in order to add 5-year follow-up overall survival (OS) data from patients included in study SG035-0004, a phase 2 open-label study of brentuximab vedotin in the treatment of patients with relapsed or refractory systemic anaplastic large cell lymphoma (ALCL), in accordance with specific obligation SOB 028. Annex II of the product information and the RMP (version 9.0) are updated accordingly

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

5.3.8. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0015

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4, 4.5, 4.8 and 5.2 of the SmPC in order to update the safety information based on the primary pharmacokinetic (PK) and preliminary safety results of food effect study CLDK378A2112: a multicentre, randomized open label study to assess the systemic exposure, efficacy, and safety of 450 mg ceritinib taken with a low-fat meal and 600 mg ceritinib taken with a low-fat meal as compared with that of 750 mg ceritinib taken in the fasted state in adult patients with anaplastic lymphoma kinase (ALK) rearranged (ALK-positive) metastatic non-small cell lung cancer (NSCLC). 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

5.3.9. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0060

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.6 of the SmPC in order to update the information on pregnancy and lactation based on two pharmacokinetic (PK) studies evaluating the transfer of Cimzia into breastmilk (UP0016 study: a multicentre, post-marketing study to evaluate the concentration of certolizumab pegol in the breast milk of mothers receiving treatment with Cimzia phase 1B (clinical pharmacology) study) and via the placenta (UP0017 study: a multicentre post-marketing study to evaluate the placental transfer of certolizumab pegol in pregnant women receiving treatment with Cimzia). The Package Leaflet and the RMP (version 12) are updated accordingly

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

5.3.10. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/X/0055/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped application consisting of: 1) line extension to introduce a new pharmaceutical form associated with new strengths (1 mg, 2.5 mg and 5 mg hard capsules), 2) type II variation to include paediatric use in the approved indication. As a consequence, sections 4.2 and 4.4 of the SmPC are updated to detail the posology in paediatric patients and to update the safety information respectively. The Package Leaflet, Labelling and the RMP (version 7.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the product information is brought in line with the latest QRD template (version 10)

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

5.3.11. Daclizumab - ZINBRYTA (CAP) - EMEA/H/C/003862/II/0007

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add 'autoimmune haemolytic anaemia' with a frequency uncommon and to include a warning concerning symptoms of this adverse drug reaction. The Package Leaflet and the RMP (version 5.0) are updated accordingly. In addition, the MAH took the opportunity to implement minor editorial amendments throughout the Product Information

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

5.3.12. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/X/0054

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Extension application for a new pharmaceutical form (Exjade 90, 180 and 360 mg granules). The RMP (version 15.0) is updated accordingly

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

5.3.13. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0062

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 4.8 of the SmPC to update the safety information and reflect the possible occurrence of multiple vertebral fractures (MVF) particularly in patients with a history of vertebral fracture following discontinuation of Prolia treatment. This results from an analysis of osteoporosis-related fracture data in subjects who discontinued investigational product and remained on study in either the Prolia phase III pivotal fracture study (study 20030216: evaluation of denosumab in the treatment of postmenopausal osteoporosis FREEDOM (fracture reduction evaluation of denosumab in osteoporosis every 6 months)) or its study extension (study 20060289: open label, single arm, extension study to evaluate the long term safety and sustained efficacy of denosumab in the treatment of postmenopausal osteoporosis) to better understand the incidence of fracture following treatment discontinuation. The Package Leaflet is updated accordingly. The RMP (version 16.0) is also updated to reflect MVF as a new important risk. In addition, the product information is updated in line with the QRD template latest version and corrected to remove typographical errors and implement minor changes in the list of local representatives

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

5.3.14. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0068

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk of fracture as well as the prevention of osteoporosis in women and men at increased risk of fracture who are starting or have recently started long-term glucocorticoid therapy. As a consequence,

sections 4.1 and 5.1 of the SmPC are updated to reflect the new indications based on the analysis of the data from the pivotal study glucocorticoid-induced osteoporosis (GIOP): study 20101217: a randomized, double-blind, active controlled study evaluating the efficacy and safety of denosumab compared with risedronate in glucocorticoid-treated individuals. The Package Leaflet and the RMP (version 19.0) are updated accordingly

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

5.3.15. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0069

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.8 of the SmPC in order to update the safety information as cataract is no longer considered to be a potential risk and/or adverse reaction associated with denosumab therapy following the completion of study 20080560 (a phase 3, multicentre, randomized, double-blind, placebo-controlled study in men to evaluate new or worsening lens opacifications in subjects with non-metastatic prostate cancer receiving denosumab for bone loss due to androgen deprivation therapy and progression study using a slit-lamp-based evaluation system (lens opacities classification system III (LOCS III)). The Package Leaflet is updated accordingly. In addition, the RMP (version 20.0) is updated to remove the important potential risk of 'cataract in men with prostate cancer receiving androgen deprivation therapy'

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

5.3.16. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0090, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include the 'treatment of refractory generalised myasthenia gravis (gMG) patients who are antiacetylcholine receptor (AChR) antibody-positive'. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated to include information on the new indication and to include the new methodology to calculate adverse drug reaction frequencies. 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. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/II/0005/G

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Julie Williams

Scope: Grouped variations consisting of: 1) update of section 4.4. of the SmPC to add a warning on the risk of lower limb amputations to align the product information (PI) with the outcome of the completed referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1442) on the risk of lower limb amputation for sodium-glucose co-transporter-2 (SGLT2) inhibitors. The Package Leaflet is updated accordingly; 2) update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC to update the PI with data from study 1245.25 Emp-Reg: a phase III, multicentre, international, randomised, parallel group,

double blind cardiovascular safety study of empagliflozin (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus (T2DM) patients with increased cardiovascular risk. The RMP (version 2.0) is updated accordingly

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

5.3.18. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/II/0026

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final results of a non-clinical study on the effect of empagliflozin on blood ketone level at refeeding after a fasting period, comparison between refeeding with glucose or fat in order to fulfil MEA 010. The RMP (version 11.0) is updated accordingly

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

5.3.19. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/II/0035

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.4 and 4.8 of the SmPC to reflect the final results of PASS CL-9785-0403 (UPWARD): a multicentre, single-arm, open-label, post-marketing safety study to evaluate the risk of seizure among subjects with metastatic castration-resistant prostate cancer (mCRPC) treated with enzalutamide who are at potential increased risk of seizure (RMP category 3). The RMP (version 11.0) is updated accordingly. In addition, the MAH took the opportunity to introduce a correction in section 5.1 of the SmPC

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

5.3.20. Fulvestrant - FASLODEX (CAP) - EMEA/H/C/000540/II/0057

Applicant: AstraZeneca UK Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of postmenopausal women with locally advanced or metastatic breast cancer who have not received prior endocrine therapy for Faslodex. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated in order to update the safety and pharmacodynamics information. The Package Leaflet and the RMP (version 10) are updated accordingly. In addition, the MAH took the opportunity to introduce clarifications in the SmPC

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

5.3.21. Fulvestrant - FASLODEX (CAP) - EMEA/H/C/000540/II/0059

Applicant: AstraZeneca UK Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the use of Faslodex in combination with palbociclib

for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in women who have received prior endocrine therapy. In pre- or peri-menopausal women, the combination treatment with palbociclib should be combined with a luteinizing hormone releasing hormone (LHRH) agonist for Faslodex. As a consequence, sections 4.1, 4.2, 4.4, 5.1, 5.3 and 6.6 of the SmPC are updated to update the safety and efficacy information. The Package Leaflet and the RMP (version 11) are updated accordingly

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

5.3.22. Human coagulation factor VIII, human von Willebrand factor - VONCENTO (CAP) - EMEA/H/C/002493/II/0017/G

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sabine Straus

Scope: Grouped variations consisting of an update of section 4.8 of the SmPC in order to amend the frequencies of undesirable effects to reflect the final clinical study report (CSR) from study CSLCT-BIO-08-53: a phase III, open-label, multicentre study to evaluate efficacy, pharmacokinetics, and safety of Voncento in paediatric subjects with haemophilia A. The Package Leaflet and the RMP (version 6.1) are updated accordingly. The revised RMP also includes the removal of the commitment to conduct a post-marketing study for haemophilia A patients (study CSLCT-BIO-12-78) for Voncento as a consequence of new data from study CSLCT-BIO-08-53. In addition, the MAH took the opportunity to combine different strengths in the SmPC and Package Leaflet

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

5.3.23. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0033/G, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 5.1 of the SmPC in order to update the safety information related to bleeding related events based on final results from study PCYC-1132-NT (RMP, category 3 (MEA 004.1) study): an in-vitro study to evaluate the effect of ibrutinib on platelet aggregation. The Package Leaflet is updated accordingly; 2) update of section 4.4 and 4.5 of the SmPC in order to update the safety information based on the final results from study LYM1003 (RMP, category 3 (MEA 009.1) study): a drug-drug interaction study to assess steady state pharmacokinetic (PK) of repeated oral doses of ibrutinib alone in patients with B-cell malignancies and when combined with a moderate and strong CYP3A[8] inhibitor. The Package Leaflet is updated accordingly; 3) update of section 4.5 of the SmPC in order to update the safety information based on the final results from study FK12024: a drug-drug interaction (DDI) study with CYP3A inhibitor posaconazole in simulated subjects. The Package Leaflet is updated accordingly; 4) update of section 4.4 of the SmPC in order to update the safety information on antimicrobial prophylaxis following routine pharmacovigilance activity; 5) update of the RMP in order to extend the closure date of study PCYC-1112-CA (ANX 003.2: a randomized, multicentre, open-label, phase 3 study of the Bruton's tyrosine kinase (BTK) inhibitor

[8] Cytochrome P450, family 3, subfamily A

ibrutinib (PCI-32765) versus ofatumumab in patients with relapsed or refractory chronic lymphocytic leukaemia/small lymphocytic lymphoma) to Q2 2019. Yearly updates will be submitted in Q2 2017 and Q2 2018. Annex II has been updated accordingly; 6) update of the RMP to include an additional action for study PCI-32765 CAN3001 (MEA017) to provide a 'further interim report in 5 years' from the time of the cut-off date of the current report (12 November 2015)' as agreed in the CHMP outcome for procedure EMA/H/C/003791/MEA 017. The RMP (version 6.8) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

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

5.3.24. Insulin detemir - LEVEMIR (CAP) - EMEA/H/C/000528/II/0084

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Doris Stenver

Scope: Submission of the summary analysis report on the incidence of neoplasms with the combination of liraglutide and insulin detemir from the cardiovascular outcome trial for Victoza (liraglutide): study EX2211-3748 (LEADER: liraglutide effect and action in diabetes): a long-term, multicentre, international, randomised double-blind, placebo-controlled trial to determine liraglutide effects on cardiovascular events. The RMP (version 18) is updated accordingly to delete the important potential risk of malignant neoplasms following combination treatment with insulin detemir, liraglutide and metformin

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

5.3.25. Insulin glargine - ABASAGLAR (CAP) - EMEA/H/C/002835/II/0014

Applicant: Eli Lilly Regional Operations GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Submission of the final report from study I4L-MC-ABER (ABER): 'a prospective, randomized, open-label comparison of long-acting basal insulin analog Abasaglar (LY2963016) to the reference product (Lantus (insulin glargine)) in adult patients with type 2 diabetes mellitus (T2DM): the ELEMENT 5 study' conducted in non-European countries. This study replaces the cancelled studies initially planned to be conducted in China and other countries. The RMP (version 1.6) is updated accordingly

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

5.3.26. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/WS1158/0154/G; LIPROLOG (CAP) - EMEA/H/C/000393/WS1158/0117/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Grouped variation consisting of: 1) addition of a pre-filled pen: Humalog and Liprolog 100 U/mL Junior KwikPen to administer insulin in half unit increments and containing insulin lispro 3mL cartridge already approved for use; 2) addition of a new pack size of 10 (2x5) pre-filled pens (multipack) for Humalog and Liprolog 100 U/mL Junior KwikPen, including insulin lispro 3mL cartridge already approved for use; 3) update of

sections 4.2 and 4.4 of the SmPC of the already authorised 100 U/mL Humalog and Liprolog presentations to include the paediatric population. The Package Leaflet and the RMP (version 8.0) are updated accordingly

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

5.3.27. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0044

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in children and adolescents 12 years of age and older. As a consequence sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 15) are updated accordingly

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

5.3.28. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0047/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Grouped variations consisting of: 1) update of section 4.4 to revise the current warning on concurrent administration with vemurafenib to enhance awareness on the potential of hypersensitivity reactions when ipilimumab is used sequentially with vemurafenib as requested by the PRAC following the assessment of PSUSA/00009200/201603 completed in October 2016; 2) update of section 4.8 of the SmPC to amend the frequency of the adverse drug reaction (ADR) 'Vogt-Konyanagi-Haranda syndrome' from 'not know' to 'very rare'. The RMP (version 16) is updated accordingly. In addition, the MAH took the opportunity to implement some editorial changes to sections 4.2 and 4.4 of the SmPC to update the dose modification information for hepatotoxicity management guidelines in line with the National Cancer Institute (NCI) common terminology criteria for adverse events (CTCAE) recommendations (version 4)

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

5.3.29. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/II/0011

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to reflect the clinical study results of the LEADER study (EX2211-3748, category 3 study): liraglutide effect on and action in diabetes - evaluation of cardiovascular outcome results to specifically address the important potential risk of cardiovascular disorders in patients with type 2 diabetes mellitus (T2DM)). The Package Leaflet, labelling and RMP (version 27) are updated accordingly. This variation application fulfils two post-approval commitments in relation to the cardiovascular outcomes trial (MEA 002), as well as providing additional information on the breast cancer cases reported in the LEADER study (MEA 005). Finally, the MAH took the opportunity to implement minor editorial changes throughout the product information

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

5.3.30. Liraglutide - VICTOZA (CAP) - EMEA/H/C/001026/II/0042

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the prevention of major adverse cardiovascular events (MACE) in adults with type 2 diabetes mellitus (T2DM) at high cardiovascular risk and as an adjunct to standard of care therapy in section 4.1 of the SmPC implementing the clinical study results of the LEADER study (EX2211-3748): liraglutide effect on and action in diabetes, evaluation of cardiovascular outcome results (category 3 study: to specifically address the important potential risk of cardiovascular disorders in patients with T2DM). As a consequence, sections 4.2, 4.4, 4.7, 4.8, 5.1 and 6.5 of the SmPC, the Package Leaflet, Labelling and RMP (version 27) are updated accordingly

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

5.3.31. Lopinavir, ritonavir - KALETRA (CAP) - EMEA/H/C/000368/II/0161/G

Applicant: AbbVie Ltd.

PRAC Rapporteur: Caroline Laborde

Scope: Grouped variation including: 1) extension of indication to include children aged 14 days and older in the treatment of human immunodeficiency virus (HIV)-1. As a consequence, sections 4.1, 4.2, 4.3, 4.8, 5.1 and 5.2 of the SmPC are updated. The studies provided in support of the paediatric indication are part of the agreed paediatric investigation plan (PIP) decision P/0144/2012. In addition, the MAH further updated section 4.4 to add information regarding the use of Kaletra oral solution with feeding tubes. The Package Leaflet, Labelling and RMP (version 8) are updated accordingly; 2) addition of a new pack size of 120 mL in (2 x 60mL bottles) for Kaletra 80mg/ml and 20 mg/ml oral solution (EU/1/01/172/003); 3) addition of a new 2 mL oral dose syringe for the 120 mL presentation

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

5.3.32. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/II/0021

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

Scope: Update of section 4.8 of the SmPC in order to add information on respiratory events based on final results from study VX14-809-106 (study 106): a Phase 3b, open-label study to evaluate the safety and tolerability of lumacaftor/ivacaftor combination therapy in subjects aged 12 years and older with cystic fibrosis and advanced lung disease homozygous for the F508del-cystic fibrosis transmembrane conductance regulator (CFTR) mutation. This study report is submitted to fulfil MEA 002. The RMP (version 3.2) is updated accordingly

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

5.3.33. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/II/0044/G, Orphan

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Update of section 4.4 of the SmPC in order to amend the warning regarding antibody response to injected insulin-like growth factor 1 (IGF-1). The RMP (version 9) is updated accordingly, including changes to the educational materials and changes to the instructions for antibody testing

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

5.3.34. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0017

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from phase 1 study NaltrexBuprop-1001 (TQT) to evaluate the potential effect of naltrexone/bupropion extended-release combination on cardiac repolarisation in healthy subjects. The RMP (version 10) is updated to include study NaltrexBuprop-1001 and additional studies recently completed (NB-CVOT (a multicentre, randomized, double-blind, placebo-controlled study assessing the occurrence of major adverse cardiovascular events (MACE) in overweight and obese subjects with cardiovascular risk factors receiving naltrexone sustained release (SR)/bupropion SR), NaltrexBuprop-4001 (a multicentre, randomized, double-blind, placebo-controlled, phase 4 study to assess the effect of naltrexone hydrochloride and bupropion hydrochloride extended release (ER) combination on the occurrence of MACE in overweight and obese subjects with cardiovascular disease), NaltrexBuprop-1004 (a phase 1, open-label, sequential design study to evaluate the potential effect of multiple oral doses of ER combination of naltrexone and bupropion on the pharmacokinetics (PK) of a single oral dose of metformin in healthy subjects) and NB-404 (a multicentre, randomized, open-label, controlled, method-of-use study assessing the effect of naltrexone SR/bupropion SR on body weight and cardiovascular risk factors in overweight and obese subjects (the Ignite study)). The MAH also took the opportunity to update the RMP to include references to the PASS protocols currently under discussion at PRAC

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

5.3.35. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0029

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of hepatocellular carcinoma after prior sorafenib therapy in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP (version 8.0) are updated accordingly

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

5.3.36. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0030

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of adults with mismatch repair deficient (dMMR) or microsatellite instability high (MSI-H) metastatic colorectal cancer after prior fluoropyrimidine based therapy. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated in order to add the new indication and update the safety information. 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

5.3.37. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/II/0093/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Grouped variations consisting of: 1) addition of a new device: the on-body injector (Onpro kit) to be used with Neulasta, 6mg solution for injection, pre-filled syringe; 2) change the fill volume for Neulasta, 6 mg, solution for injection pre-filled syringe co-packed with the on-body injector (Onpro kit). In addition, the MAH took the opportunity to introduce editorial changes to module 3.2.P.2.4 on container closure system. As a consequence, sections 3, 4.2, 5.1, 6.4, 6.5, 6.6 and 8 of the SmPC are updated. The Labelling, Package Leaflet and the RMP (version 4.2) are updated accordingly. In addition the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to include some editorial changes and correct some typos throughout the product information. Finally, the MAH brought 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

5.3.38. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0027

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include first line treatment of metastatic non-squamous non-small cell lung cancer (NSCLC) in combination with platinum-pemetrexed chemotherapy based on the results from study KEYNOTE-021 (cohort G): a Phase 1/2, open-label trial of pembrolizumab in combination with chemotherapy or immunotherapy in patients with locally advanced or metastatic NSCLC. As a consequence sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.39. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0028

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.4 and 4.8 of the SmPC to include the risk of myocarditis reported in patients treated with pembrolizumab. The Package Leaflet and the RMP (version 10.0) are updated accordingly

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

5.3.40. Pertuzumab - PERJETA (CAP) - EMEA/H/C/002547/II/0029

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 of the SmPC, Annex II and relevant sections of the Packet Leaflet in order to update information on cardiac safety and reflect the results from study BERENICE (WO29217) listed as a specific obligation in Annex II: an ongoing multicentre, multinational, phase II study to evaluate Perjeta in combination with trastuzumab and standard neoadjuvant anthracycline-based chemotherapy in patients with human epidermal growth factor receptor 2 (HER2)-positive, locally advanced, inflammatory, or early-stage breast cancer. The RMP (version 9) is updated accordingly

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

5.3.41. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/II/0004/G, Orphan

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations to update sections 4.4, 4.5, 4.6 and 5.2 of the SmPC based on the final clinical study report (CSR) of study P15-02 assessing the mass balance recovery, metabolite profile and metabolite identification of [^{14}C] pitolisant at steady state conditions, in healthy cytochrome P450 2D6 (CYP2D6) phenotyped subjects, study P14-07 evaluating the pharmacokinetic interaction of pitolisant with sodium oxybate and modafinil in healthy male volunteers and study P15-15 evaluating the pharmacokinetic (PK) interaction of pitolisant with cytochrome P450 3A4 (CYP3A4) substrates (midazolam), cytochrome P450 2B6 (CYP2B6) substrates (bupropion), UDP-Glucuronosyltransferase-2B7 (UGT2B7) inhibitors (probenecide)) in fulfilment of PAM (MEA 02, 03 and 04). The Package Leaflet and the RMP (version 5.0) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial change in section 4.8 of the SmPC

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

5.3.42. Regorafenib - STIVARGA (CAP) - EMEA/H/C/002573/II/0020

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with one systemic therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and RMP (version 5.0) are updated accordingly. 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

5.3.43. Rilpivirine - EDURANT (CAP) - EMEA/H/C/002264/II/0024

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 SmPC in order to include information: use of rilpivirine in combination with a background regimen for the treatment of human immunodeficiency virus (HIV)-1 infection during pregnancy and postpartum, without dose adjustment following final results from study TMC114HIV3015 (a single arm, open-label trial to assess the pharmacokinetics of darunavir/ritonavir, etravirine, and rilpivirine in HIV-1-infected pregnant women) listed as a category 3 study in the RMP. The Package Leaflet and the RMP (version 7.0) are updated accordingly. In addition, the MAH took the opportunity to introduce the latest renewal date in section 9 of the SmPC and the physical address of the Netherlands local representative in the Package Leaflet

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

5.3.44. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/II/0017/G

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variation consisting of: 1) update of sections 4.2, 4.8 and 5.1 of the SmPC to reflect available data from previously untreated patients (PUP) based on the interim report of interventional study GENA-05 (an immunogenicity, efficacy and safety of treatment with human cell line-derived recombinant factor VIII (human-cl-rhFVIII) in previously untreated patients with severe haemophilia A). The Package Leaflet and the RMP (version 8.0) are updated accordingly. In addition, the MAH took the opportunity to update the product information throughout to bring it in line with the core SmPC for human plasma-derived and recombinant coagulation factor VIII products (EMA/CHMP/BPWP/1619/1999 rev. 2) and with the latest QRD template (version 10). Moreover, the MAH proposed to combine the SmPC for all strengths and to update Annex A with detailed information on the packaging

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

5.3.45. Sitagliptin - JANUVIA (CAP) - EMEA/H/C/000722/WS1141/0056; RISTABEN (CAP) - EMEA/H/C/001234/WS1141/0048; TESAVEL (CAP) - EMEA/H/C/000910/WS1141/0056; XELEVIA (CAP) - EMEA/H/C/000762/WS1141/0060

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.4 of the SmPC in order to add 'bullous pemphigoid' as a warning following the PRAC outcome for EMEA/H/C/PSUSA/2711/201408 procedure completed in 2015. The Labelling and the RMP (version 7) are updated accordingly

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

5.3.46. Sitagliptin, metformin hydrochloride - EFFICIB (CAP) - EMEA/H/C/000896/WS1130/0081/G; JANUMET (CAP) - EMEA/H/C/000861/WS1130/0081/G; RISTFOR (CAP) - EMEA/H/C/001235/WS1130/0068/G; VELMETIA (CAP) - EMEA/H/C/000862/WS1130/0084/G

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variation consisting of: 1) update of section 4.4 of the SmPC in order to add 'bullous pemphigoid' as a warning following the PRAC outcome for EMEA/H/C/PSUSA/2711/201408 procedure. The Labelling and the RMP (version 7) are updated accordingly; 2) The RMP (version 7) is updated to add a targeted questionnaire related to lactic acidosis as part of the outcome of a referral procedure under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1432) on metformin-containing medicines completed in 2016

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

5.3.47. Sulphur hexafluoride - SONOVUE (CAP) - EMEA/H/C/000303/X/0034/G

Applicant: Bracco International B.V.

PRAC Rapporteur: Claire Ferard

Scope: Grouped application consisting of: 1) line extension to introduce intravesical use as a new route of administration; 2) type II variation to add a new indication to include the use in ultrasonography of the excretory urinary tract in paediatric patients to detect or exclude vesicoureteral reflux. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 6 of the SmPC are updated. The Package Leaflet and the RMP (version 9.1) are updated accordingly. In addition, the MAH took the opportunity to bring Annex IIIA in line with the latest QRD template (version 10)

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

5.3.48. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0066

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the use in adult patients for the treatment of giant cell arteritis for the subcutaneous formulation of RoActemra. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated to reflect information relevant to this indication. The Package Leaflet and the RMP (version 21) are updated accordingly

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

5.3.49. Varenicline - CHAMPIX (CAP) - EMEA/H/C/000699/II/0064

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: Update of sections 4.5 and 5.1 of the SmPC in order to update the safety information based on the final results from study A3051078: a varenicline pregnancy cohort study (a prospective population-based cohort study to examine whether varenicline use during pregnancy is associated with an increased risk of major congenital malformations in infants above that associated with smoking during pregnancy). The Package Leaflet and the RMP (version 10.1) are updated accordingly. In addition, the MAH took the opportunity to bring the Product Information in line with the latest QRD template (version 10)

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

5.3.50. Varenicline - CHAMPIX (CAP) - EMEA/H/C/000699/II/0066

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: Update of section 5.1 of the SmPC in order to update the safety information based on the final results from clinical study A3051148 (a phase 4, non-treatment follow-up for cardiac assessments following use of smoking cessation treatments in subjects with and without a history of psychiatric disorders), a non-treatment extension to study A3051123, to collect data on cardiovascular safety for all participants in study A3051123 (a phase 4, randomized, double-blind, active and placebo-controlled, multicentre study evaluating the neuropsychiatric safety and efficacy of 12 weeks varenicline tartrate 1mg twice a day (bid) and bupropion hydrochloride 150mg bid for smoking cessation in subjects with and without a history of psychiatric disorders) for an additional 28 weeks, allowing for a total of 52 weeks of cardiovascular safety data collection. The RMP (version 10.1) is updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Aclidinium bromide, formoterol - BRIMICA GENUAIR (CAP), DUAKLIR GENUAIR (CAP) - PSUSA/00010307/201611

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Aflibercept[9] - EYLEA (CAP) - PSUSA/00010020/201611

Applicant: Bayer AG

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Albutrepenonacog alfa - IDELVION (CAP) - PSUSA/00010497/201611

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Autologous $CD34^+$ enriched cell fraction that contains $CD34^+$ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) complementary deoxyribonucleic acid (cDNA) sequence - STRIMVELIS (CAP) - PSUSA/00010505/201611

Applicant: GlaxoSmithKline Trading Services; ATMP[10]

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.5. Cabozantinib - CABOMETYX (CAP); COMETRIQ (CAP) - PSUSA/00010180/201611

Applicant: Ipsen Pharma

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Carbidopa, levodopa[11] - NUMIENT (CAP) - PSUSA/00010479/201611

Applicant: Impax Laboratories Ireland Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] For wet macular degeneration and central retinal vein occlusion (CRVO) indications only
[10] Advanced therapy medicinal product
[11] Centrally authorised product only

6.1.7. Ceftaroline fosamil - ZINFORO (CAP) - PSUSA/00010013/201610

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Ceritinib - ZYKADIA (CAP) - PSUSA/00010372/201610

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Cobicistat, darunavir - REZOLSTA (CAP) - PSUSA/00010315/201611

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - PSUSA/00010449/201611

Applicant: Gilead Sciences International Ltd

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/00000873/201610

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. Daclizumab - ZINBRYTA (CAP) - PSUSA/00010518/201611

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Dalbavancin - XYDALBA (CAP) - PSUSA/00010350/201611

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Daratumumab - DARZALEX (CAP) - PSUSA/00010498/201611

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Deferasirox - EXJADE (CAP) - PSUSA/00000939/201610

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Elotuzumab - EMPLICITI (CAP) - PSUSA/00010500/201611

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Eribulin - HALAVEN (CAP) - PSUSA/00001254/201611

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Fentanyl[12] - IONSYS (CAP) - PSUSA/00010453/201611

Applicant: Incline Therapeutics Europe Ltd

[12] Transdermal system - centrally authorised product

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Flutemetamol (^{18}F) - VIZAMYL (CAP) - PSUSA/00010293/201610

Applicant: GE Healthcare Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Glycerol phenylbutyrate - RAVICTI (CAP) - PSUSA/00010454/201611

Applicant: Horizon Pharma Ireland Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - CERVARIX (CAP) - PSUSA/00009175/201611

Applicant: GSK Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Hydrocortisone[13] - PLENADREN (CAP) - PSUSA/00009176/201611

Applicant: Shire Services BVBA

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ibrutinib - IMBRUVICA (CAP) - PSUSA/00010301/201611 (with RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[13] Adrenal insufficiency, modified-release tablets only

6.1.24. Insulin detemir - LEVEMIR (CAP) - PSUSA/00001750/201610 (with RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Ketoconazole[14] - KETOCONAZOLE HRA (CAP) - PSUSA/00010316/201611

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Levofloxacin[15] - QUINSAIR (CAP) - PSUSA/00010429/201611

Applicant: Horizon Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Lidocaine, prilocaine[16] - FORTACIN (CAP) - PSUSA/00010110/201611

Applicant: Plethora Solutions Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Lumacaftor, ivacaftor - ORKAMBI (CAP) - PSUSA/00010455/201611 (with RMP)

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Metformin, saxagliptin - KOMBOGLYZE (CAP) - PSUSA/00002686/201611

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

[14] Centrally authorised product only
[15] Centrally authorised product only
[16] Centrally authorised product only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Migalastat - GALAFOLD (CAP) - PSUSA/00010507/201611

Applicant: Amicus Therapeutics UK Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - VELPHORO (CAP) - PSUSA/00010296/201611

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Necitumumab - PORTRAZZA (CAP) - PSUSA/00010471/201611

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Nintedanib[17] - VARGATEF (CAP) - PSUSA/00010318/201611

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Agni Kapou

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Obinutuzumab - GAZYVARO (CAP) - PSUSA/00010279/201610

Applicant: Roche Registration Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[17] Oncology indication(s) only

6.1.35. Osimertinib - TAGRISSO (CAP) - PSUSA/00010472/201611

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 MEDIMMUNE (CAP) - PSUSA/00010501/201611

Applicant: MedImmune LLC

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Pixantrone - PIXUVRI (CAP) - PSUSA/00009261/201611

Applicant: CTI Life Sciences Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Radium (^{223}Ra) dichloride - XOFIGO (CAP) - PSUSA/00010132/201611

Applicant: Bayer AG

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Rituximab - MABTHERA (CAP) - PSUSA/00002652/201611

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Rotavirus vaccine pentavalent (live, oral) - ROTATEQ (CAP) - PSUSA/00002666/201611

Applicant: MSD Vaccins

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Sapropterin - KUVAN (CAP) - PSUSA/00002683/201612 (with RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Simeprevir - OLYSIO (CAP) - PSUSA/00010255/201611

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Stiripentol - DIACOMIT (CAP) - PSUSA/00002789/201611

Applicant: Biocodex

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Susoctocog alfa - OBIZUR (CAP) - PSUSA/00010458/201611

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Tadalafil - ADCIRCA (CAP), CIALIS (CAP), NAP - PSUSA/00002841/201610 (with RMP)

Applicant: Eli Lilly Nederland B.V. (Adcirca, Cialis)

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Tilmanocept - LYMPHOSEEK (CAP) - PSUSA/00010313/201611

Applicant: Norgine BV

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Tolvaptan[18] - JINARC (CAP) - PSUSA/00010395/201611

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Trametinib - MEKINIST (CAP) - PSUSA/00010262/201611

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Turoctocog alfa - NOVOEIGHT (CAP) - PSUSA/00010138/201610

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Vedolizumab - ENTYVIO (CAP) - PSUSA/00010186/201611

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Zinc acetate dihydrate - WILZIN (CAP) - PSUSA/00003145/201610

Applicant: Orphan Europe S.A.R.L.

PRAC Rapporteur: Almath Spooner

[18] Adults with autosomal dominant polycystic kidney disease (ADPKD) indication only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Interferon alfa-2b - INTRONA (CAP), NAP - PSUSA/00001758/201609

Applicants: Merck Sharp & Dohme Limited (IntronA), various

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Irbesartan, hydrochlorothiazide - COAPROVEL (CAP), IRBESARTAN HYDROCHLOROTHIAZIDE ZENTIVA (CAP), KARVEZIDE (CAP), NAP - PSUSA/00001653/201609

Applicants: Sanofi Clir SNC (CoAprovel), Sanofi-aventis groupe (Irbesartan Hydrochlorothiazide Zentiva, Karvezide), various

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Sevelamer - RENAGEL (CAP); RENVELA (CAP), SEVELAMER CARBONATE ZENTIVA (CAP), TASERMITY (CAP), NAP - PSUSA/00002697/201610

Applicants: Genzyme Europe BV (Renagel, Renvela, Sevelamer carbonate Zentiva, Tasermity), various

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Sodium oxybate - XYREM (CAP), NAP - PSUSA/00002757/201610

Applicants: UCB Pharma Ltd. (Xyrem), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Acitretin (NAP) - PSUSA/00000051/201610

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Ambroxol (NAP) - PSUSA/00000130/201609

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Ambroxol, clenbuterol (NAP) - PSUSA/00000131/201609

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Aminosalicylate sodium (NAP) - PSUSA/00000165/201610

Applicant(s): various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Amlodipine, perindopril (NAP) - PSUSA/00000179/201610

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Artemether, lumefantrin[19] (NAP) - PSUSA/00000236/201610

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Baclofen[20] (NAP) - PSUSA/00000294/201609

Applicant: various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Brimonidine[21] (NAP) - PSUSA/00000430/201609

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Brimonidine, timolol (NAP) - PSUSA/00000431/201609

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Bromhexine (NAP) - PSUSA/00000437/201609

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Carbidopa, levodopa[22] (NAP) - PSUSA/00000548/201610

Applicant(s): various

[19] All except dispersible tablet
[20] Oral route of administration only
[21] Except centrally authorised product(s)
[22] Except centrally authorised product(s)

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Dinoprostone (NAP) - PSUSA/00001104/201609

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Erythromycin, tretinoin (NAP) - PSUSA/00001259/201610

Applicant(s): various

PRAC Lead: Tatiana Magalova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Felbamate (NAP) - PSUSA/00010155/201609

Applicant(s): various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Ivermectin[23] (NAP) - PSUSA/00010376/201610

Applicant(s): various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Letrozole (NAP) - PSUSA/00001842/201610

Applicant(s): various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[23] For topical use only

6.3.17. Levosimendan (NAP) - PSUSA/00001858/201609

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Methylphenidate (NAP) - PSUSA/00002024/201610

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Olmesartan (NAP) - PSUSA/00002207/201610

Applicant(s): various

PRAC Lead: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Olmesartan, hydrochlorothiazide (NAP) - PSUSA/00000179/201610

Applicant(s): various

PRAC Lead: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Rabeprazole (NAP) - PSUSA/00002601/201610

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Technetium (^{99m}Tc) bicisate (NAP) - PSUSA/00002856/201610

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Tetrabenazine (NAP) - PSUSA/00002911/201610

Applicant(s): various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Timolol[24] (NAP) - PSUSA/00010432/201610

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Tiotropium (NAP) - PSUSA/00002972/201610

Applicant(s): various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Anakinra - KINERET (CAP) - EMEA/H/C/000363/LEG 028

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of a review on the feasibility of conducting a PASS in order to evaluate the risk of adverse cardiovascular events associated with long-term use of anakinra in patients with rheumatoid arthritis (RA) as requested in the conclusions of EMEA/H/C/PSUSA/00000209/201605 adopted by PRAC in December 2016

Action: For adoption of advice to CHMP

6.4.2. Mycophenolate mofetil - CELLCEPT (CAP) - EMEA/H/C/000082/LEG 039

Applicant: Roche Registration Limited

PRAC Rapporteur: Patrick Batty

Scope: Submission of a justification on the need for two forms of contraception and any

[24] For systemic use only

evidence for non-compliance with these requirements leading to unintended pregnancy; a detailed review of all known clinical data of reported malformations from paternal cases; a review of available non-clinical data relating to the potential for male-mediated developmental toxicity as requested in the conclusions of EMEA/H/C/PSUSA/00002099/201605 adopted by PRAC in December 2016

Action: For adoption of advice to CHMP

6.4.3. Orlistat - ALLI (CAP) - EMEA/H/C/000854/LEG 027

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Julie Williams

Scope: Submission of a detailed safety review on all case reports of nephrotoxicity for both orlistat 60 mg and orlistat 120 mg as requested in the conclusions of EMEA/H/C/PSUSA/00002220/201602 adopted by PRAC in September 2016

Action: For adoption of advice to CHMP

6.4.4. Orlistat - XENICAL (CAP) - EMEA/H/C/000154/LEG 026

Applicant: Cheplapharm Arzneimittel GmbH

PRAC Rapporteur: Caroline Laborde

Scope: Submission of a detailed safety review on all case reports of nephrotoxicity for both orlistat 60 mg and orlistat 120 mg as requested in the conclusions of EMEA/H/C/PSUSA/00002220/201602 adopted by PRAC in September 2016

Action: For adoption of advice to CHMP

6.4.5. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/LEG 005

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Eva Segovia

Scope: Submission of a detailed review on suicidal ideation and behaviour providing preclinical, clinical, epidemiology and post-marketing data as requested in the conclusions of EMEA/H/C/PSUSA/00010341/201606 adopted by PRAC in January 2017

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[25]

7.1.1. Aclidinium bromide – EKLIRA GENUAIR (CAP), BRETARIS GENUAIR (CAP); aclidinium bromide, formoterol – DUAKLIR GENUAIR (CAP), BRIMICA GENUAIR (CAP) - EMEA/H/C/PSA/S/0017

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Submission of a substantial amendment to the protocol for the aclidinium bromide PASS evaluating the potential for cardiovascular safety concerns and all-cause mortality described in the RMP, through sequential, nested case-control studies for each endpoint of interest

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

7.1.2. Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - ZALMOXIS (CAP) - EMEA/H/C/PSP/S/0055

Applicant: MolMed SpA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of a protocol for study TK011: a prospective, non-interventional PASS on long-term safety and effectiveness in patients undergoing haploidentical hematopoietic stem cell transplantation for high-risk haematological malignancies

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

7.1.3. Ketoconazole – KETOCONAZOLE HRA (CAP) - EMEA/H/C/PSP/S/0040.3

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: Submission of a revised PASS protocol for a prospective, multinational, observational registry to collect clinical information on patients with endogenous Cushing's syndrome exposed to ketoconazole (using the existing European Registry on Cushing's syndrome (ERCUSYN)), to assess drug utilisation pattern and to document the safety (e.g. hepatotoxicity, QT prolongation) and effectiveness of ketoconazole

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

7.1.4. Lesinurad - ZURAMPIC (CAP) - EMEA/H/C/PSP/S/0050.2

Applicant: Grunenthal GmbH

[25] In accordance with Article 107n of Directive 2001/83/EC

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a revised PASS protocol for an observational post-authorisation study of lesinurad patients (SATURATES), to investigate cardiovascular risk in association with lesinurad exposure, mainly in patients with a history of cardiovascular disorders

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

7.1.5. Pomalidomide – IMNOVID (CAP) - EMEA/H/C/PSA/S/0012.1

Applicant: Celgene Europe Ltd

PRAC Rapporteur: Patrick Batty

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

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

7.1.6. Thiocolchicoside (NAP) - EMEA/H/N/PSA/J/0010.1

Applicant: Sanofi

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of a revised PASS protocol for a drug utilisation study (DUS) for thiocolchicoside (TCC)-containing medicinal products for systemic use in France and Italy: an electronic medical records database study

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[26]

7.2.1. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/MEA 050

Applicant: Teva B.V.

PRAC Rapporteur: Claire Ferard

Scope: Submission of a protocol for a post-authorisation long term safety cohort study in acute promyelocytic leukaemia (APL) patients treated with Trisenox to assess the long-term safety of all-trans retinoic acid (ATRA) + arsenic trioxide (ATO) in newly diagnosed low to intermediate risk APL patients in a real-world clinical practice setting as requested in the conclusions of variation II/0058 finalised in October 2016

Action: For adoption of advice to CHMP

7.2.2. Agomelatine - THYMANAX (CAP) - EMEA/H/C/000916/MEA 026.2

Applicant: Servier (Ireland) Industries Ltd.

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

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Submission of substantial amendments to the protocol for cross sectional study CLE-20098-96-096: a non-interventional PASS: drug utilisation study (DUS) in selected European countries: a multinational, observational study to assess the effectiveness of risk-minimisation measures

Action: For adoption of advice to CHMP

7.2.3. Agomelatine - VALDOXAN (CAP) - EMEA/H/C/000915/MEA 026.2

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Submission of substantial amendments to the protocol for cross sectional study CLE-20098-96-096: a non-interventional PASS: drug utilisation study (DUS) in selected European countries: a multinational, observational study to assess the effectiveness of risk-minimisation measures

Action: For adoption of advice to CHMP

7.2.4. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 007.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of the MAH's response to MEA 007 [submission of a non-clinical mechanistic study protocol in dogs to investigate the mechanism behind canagliflozin-containing medicines induced diabetic ketoacidosis occurrence, as per the outcome of the recently finalised procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA)] as per the request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.5. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 006.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of the MAH's response to MEA 006 [submission of a non-clinical mechanistic study protocol in dogs to investigate the mechanism behind canagliflozin-containing medicines induced diabetic ketoacidosis occurrence, as per the outcome of the recently finalised procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA)] as per the request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.6. Collagenase clostridium histolyticum - XIAPEX (CAP) - EMEA/H/C/002048/MEA 030.1

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of the MAH's response to MEA 030 relating to protocol amendments [protocol for study Sobi.Xiapex-PASS02: a non-interventional PASS measuring the effectiveness of Xiapex educational material for healthcare professional in the treatment of Dupuytren's contracture (as per the conclusions of variation II/59)] as per the request for supplementary information (RSI) adopted in January 2017

Action: For adoption of advice to CHMP

7.2.7. Daclizumab - ZINBRYTA (CAP) - EMEA/H/C/003862/MEA 002.1

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of the MAH's response to MEA 002 relating to an updated pregnancy registry protocol [submission of a PASS protocol for the category 3 Biogen multiple sclerosis (MS) pregnancy exposure registry 109MS402 (PASS category 3) to prospectively evaluate pregnancy outcomes in women with MS who were exposed to a registry-specified Biogen MS product during the eligibility window for that product] as per the request for supplementary information (RSI) adopted in January 2017

Action: For adoption of advice to CHMP

7.2.8. Emtricitabine, rilpivirine, tenofovir disoproxil - EVIPLERA (CAP) - EMEA/H/C/002312/MEA 011.4

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Revised protocol for study EDMS-ERI-139775027: an ongoing healthcare professionals (HCP) survey: observational cohort study to assess rilpivirine (RPV) utilisation according to the EU product information

Action: For adoption of advice to CHMP

7.2.9. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/MEA 167.2

Applicant: Pfizer Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of the MAH's response to MEA 167.1 relating to a revised PASS protocol [submission of a revised PASS protocol for study B1801396: an observational cohort study to evaluate the risk of adverse pregnancy outcomes in patients treated with etanercept compared to those not treated with etanercept or other biologics using merged data from Sweden, Denmark and Finland (as per the conclusions of variation II/184)] as per the request for supplementary information (RSI) adopted in January 2017

Action: For adoption of advice to CHMP

7.2.10. Florbetapir (^{18}F) - AMYVID (CAP) - EMEA/H/C/002422/MEA 001.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Amendment to the protocol of study I6E-AV-AVBE: a non-interventional PASS evaluating the effectiveness of Amyvid reader training programme, initially endorsed by PRAC/CHMP in December 2013, amended following the conclusions of variation II/22 finalised at CHMP in December 2016 to allow the optional use of quantitative reading as an adjunct to visual reading leading resulting in changes in the reader training programme

Action: For adoption of advice to CHMP

7.2.11. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/MEA 046.1

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of the MAH's response to MEA 046 [submission of a PASS protocol to further investigate and characterise the associations of lenalidomide and tumour flare reaction (TFR)/high tumour burden following the extension of indication for the treatment of adult patients with relapsed and/or refractory mantle cell lymphoma (RRMCL) (as per the conclusions of variation II/79) (final study report planned in December 2022)] as per the request for supplementary information (RSI) adopted in January 2017

Action: For adoption of advice to CHMP

7.2.12. Loxapine - ADASUVE (CAP) - EMEA/H/C/002400/MEA 001.2

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Sabine Straus

Scope: 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-(oxapine for inhalation) in agitated persons in routine clinical care

Action: For adoption of advice to CHMP

7.2.13. Rilpivirine - EDURANT (CAP) - EMEA/H/C/002264/MEA 011.4

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Revised protocol for study EDMS-ERI-139775027: an ongoing healthcare professionals (HCP) survey: observational cohort study to assess rilpivirine (RPV) utilisation according to the EU product information

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[27]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[28]

7.4.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0062

Applicant: Genzyme Europe BV

PRAC Rapporteur: Caroline Laborde

Scope: Submission of the final study report for ALGMYC08432: a non-interventional, non-imposed PASS entitled: 'Myozyme (alglucosidase alfa) safety information packet (SIP) effectiveness evaluation: a healthcare professional (HCP) survey' (Myozyme SIP EU HCP survey). The RMP (version 8.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Collagenase clostridium histolyticum - XIAPEX (CAP) - EMEA/H/C/002048/II/0089

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report (CSR) for B1531005: a non-interventional study to evaluate the outcomes (clinical treatment success measured by goniometry assessment, recurrence rate measured by goniometry assessment, subject and physician global assessment of treatment satisfaction, complications resulting from the procedure based on the adverse event/serious adverse event (AE/SAE)) of 3 various treatment options for Dupuytren's contracture, listed as a category 3 study in the RMP. The RMP (version 13.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/II/0025

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final results for a non-interventional study 1245.122 exploring the characteristics of patients initiating empagliflozin or other noninsulin glucose lowering drugs in the United Kingdom in order to fulfil MEA 009. The RMP (version 11.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

[27] In accordance with Article 107p-q of Directive 2001/83/EC
[28] 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

7.4.4. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - CERVARIX (CAP) - EMEA/H/C/000721/II/0088

Applicant: GSK Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final study report for study EPI-HPV-067: a PASS pregnancy registry. Data and information related to the use of Cervarix during pregnancy was identified as important missing information in the RMP

Action: For adoption of PRAC Assessment Report

7.4.5. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0201/G

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variation consisting of: 1) submission of the clinical study reports (CSR) for studies C0168T45 (safety under long term study: multicentre international observational study of the long-term safety of infliximab) and C0168T62 (safety under long-term study in ulcerative colitis (UC): multicentre international study of the long-term safety of infliximab in UC) together with an overall summary and evaluation of the complete long term safety follow-up programmes for Remicade (as per MEA 79). The RMP (version 14.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0204

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final registry report from C0168T71 study: a review and analysis of birth outcomes from Swedish, Danish and Finish medical birth registers and an evaluation of pregnancy data from multiple sources. As a consequence, section 4.6 of the SmPC is updated. The Package Leaflet and the RMP (version 13.2) are updated accordingly. In addition, the MAH took the opportunity to bring the product in line with the latest QRD template and update the local representative section of the Package Leaflet

Action: For adoption of PRAC Assessment Report

7.4.7. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/II/0002

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report from a pharmacoepidemiology study listed as a category 3 study in the RMP: a retrospective database study on glucagon-like peptide-1 (GLP-1) receptor agonists and risk of acute pancreatitis, pancreatic cancer and thyroid cancer, in particular medullary thyroid cancer, for which the primary objective was to estimate the incidence rates of acute pancreatitis, pancreatic and thyroid cancer amongst

adult patients with type 2 diabetes mellitus (T2DM) treated with GLP-1 receptor agonists versus patients treated with other antidiabetics. The RMP (version 2.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. Paliperidone - XEPLION (CAP) - EMEA/H/C/002105/II/0031

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final study report for a PASS using European Union databases to assess the risk of cardiovascular and cerebrovascular adverse events in elderly patients treated with paliperidone palmitate, paliperidone prolonged-release, and other antipsychotics

Action: For adoption of PRAC Assessment Report

7.4.9. Sodium oxybate - XYREM (CAP) - EMEA/H/C/000593/II/0066

Applicant: UCB Pharma Ltd.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study C00302 (post marketing non-interventional surveillance pharmacoepidemiology study (PMSS) to evaluate long-term safety, tolerability and compliance in administration of Xyrem (sodium oxybate) oral solution in patients who receive treatment with this medication in regular clinical practice) listed as a category 3 study in the RMP. The RMP (version 8) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.10. Sonidegib - ODOMZO (CAP) - EMEA/H/C/002839/II/0011

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Patrick Batty

Scope: Submission of the final results from study CLDE225C2301: a phase 2, multicentre, open-label, single-arm study of the efficacy and safety of oral LDE225 in patients with Hegehog (Hh)-signalling pathway activated relapsed medulloblastoma, and study LDE225X2104. a phase 1/2 study of sonidegib (LDE225) in paediatric patients with recurrent or refractory medulloblastoma or other tumours potentially dependent on the Hh-signalling pathway and adult patients with recurrent or refractory medulloblastoma. The RMP (version 6.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 046.4

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Ninth and last annual update of the rheumatoid arthritis registries: interim post-marketing epidemiology assessment report from the abatacept post-marketing epidemiology programme that includes studies whose primary focus is to evaluate the safety of abatacept for the treatment of rheumatoid arthritis (RA) (RMP category 3 - due date: final report in 2018)

Action: For adoption of advice to CHMP

7.5.2. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 048.5

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Annual report for study IM101240: 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 (due date: final registry report by 2029)

Action: For adoption of advice to CHMP

7.5.3. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 065.7

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Eighth interim report for the psoriasis patient registry (study P10-023: 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

7.5.4. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 066.6

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report from the RABBIT registry (Rheumatoide Arthritis: Beobachtung der Biologika-Therapie) for cohort 2: evaluation of safety data through 31 October 2016 from the clinical use of adalimumab

Action: For adoption of advice to CHMP

7.5.5. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.11

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fourth 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

7.5.6. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 002.5

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002.4: first interim analysis report for a US category 3, PASS (B2311060 study): active surveillance of conjugated estrogens (CE)/bazedoxifene acetate (BZA) using US healthcare data as per the request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.5.7. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 010

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: First monitoring interim report for PASS study 1245.97: a non-interventional PASS assessing the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 diabetes mellitus (T2DM): a multi-database European study

Action: For adoption of advice to CHMP

7.5.8. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 006

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: First monitoring interim report for PASS study 1245.97: a non-interventional PASS assessing the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 diabetes mellitus (T2DM): a multi-database European study

Action: For adoption of advice to CHMP

7.5.9. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/MEA 002

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Julie Williams

Scope: First monitoring interim report for PASS study 1245.97: a non-interventional PASS

assessing the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 diabetes mellitus (T2DM): a multi-database European study

Action: For adoption of advice to CHMP

7.5.10. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 002

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Patrick Batty

Scope: Annual interim report from an established nationwide register (British Society for Rheumatology Rheumatoid Arthritis Register (BSRBR-RA) for patients with rheumatological disorders treated with biologic agents, designed as a national prospective study whose primary purpose is to assess long-term toxicity from the use of these agents in routine practice

Action: For adoption of advice to CHMP

7.5.11. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 003

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Patrick Batty

Scope: Annual interim report for study from RABBIT-RA (Rheumatoide Arthritis: Beobachtung der Biologika-Therapie): a prospective, observational cohort study evaluating the long-term effectiveness, safety, and costs associated with tumour necrosis factor (TNF)-inhibitor therapies in the treatment of rheumatoid arthritis (RA) and comparing it to a cohort of RA patients treated with non-biologic disease-modifying anti-rheumatic drugs (DMARDs)

Action: For adoption of advice to CHMP

7.5.12. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 004

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Patrick Batty

Scope: Annual interim report for study from ARTIS register (Anti-Rheumatic Treatment in Sweden): a national prospective, observational, uncontrolled cohort study evaluating the risk of selected adverse events (AEs) in rheumatoid arthritis (RA), juvenile idiopathic arthritis, and other rheumatic disease patients treated with etanercept

Action: For adoption of advice to CHMP

7.5.13. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 005

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Patrick Batty

Scope: Annual interim report for study from BADBIR (British Association of Dermatologists Biologic Interventions Register): a nationwide registry assessing the long-term safety of

biologic treatments for psoriasis

Action: For adoption of advice to CHMP

7.5.14. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 008.4

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of MAH's responses to MEA 008.3 regarding the annual interim report on an i3 drug safety epidemiology study CNTO148ART4002: golimumab safety and surveillance programme using the Optum research database

Action: For adoption of advice to CHMP

7.5.15. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/MEA 028.4

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Fourth interim report of a PASS study (RMP category 3): 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 (sKPB) of Humalog and Liprolog. This fourth interim report covers the batches released to the market between 15 October 2013 and 31 January 2017

Action: For adoption of advice to CHMP

7.5.16. Insulin lispro - LIPROLOG (CAP) - EMEA/H/C/000393/MEA 021.4

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Fourth interim report of a PASS study (RMP category 3): 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 (sKPB) of Humalog and Liprolog. This fourth interim report covers the batches released to the market between 15 October 2013 and 31 January 2017

Action: For adoption of advice to CHMP

7.5.17. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/MEA 036.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Annual interim report (covering the period 1 February 2016 to 31 January 2017) on the effectiveness of risk minimisation measures for multiple patch use with copies of Council for International Organizations of Medical Sciences (CIOMS) reports of medication errors and misuse

Action: For adoption of advice to CHMP

7.5.18. Rivastigmine - PROMETAX (CAP) - EMEA/H/C/000255/MEA 037.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Annual interim report (covering the period 1 February 2016 to 31 January 2017) on the effectiveness of risk minimisation measures for multiple patch use with copies of Council for International Organizations of Medical Sciences (CIOMS) reports of medication errors and misuse

Action: For adoption of advice to CHMP

7.5.19. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 018

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: First yearly progress report (22 December 2015-27 January 2017) for study PGL14-001: a prospective, multinational, multicentre, non-interventional study to evaluate the long-term safety of Esmya in particular the endometrial safety and the current prescription and management patterns of Esmya in a long-term treatment setting

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/MEA 093.5

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of the MAH's response to MEA 093.4 on the statistical analysis plan (SAP) for the RIVAS study [PASS registry protocol for a long-term surveillance study of rituximab (Mabthera)-treated patients with granulomatosis, with polyangiitis (GPA) or microscopic polyangiitis (MPA) (RIVAS)] as per request for supplementary information (RSI) adopted in April 2017

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Amifampridine - FIRDAPSE (CAP) - EMEA/H/C/001032/S/0049 (without RMP)

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

None

8.3. Renewals of the marketing authorisation

8.3.1. Anidulafungin - ECALTA (CAP) - EMEA/H/C/000788/R/0033 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - EMEA/H/C/002246/R/0031 (with RMP)

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Valerie Strassmann

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/R/0035 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Linaclotide – CONSTELLA (CAP) - EMEA/H/C/002490/R/0032

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Valerie Strassmann

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Pioglitazone, metformin hydrochloride - GLUBRAVA (CAP) - EMEA/H/C/000893/R/0054 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Zoledronic acid - ZOLEDRONIC ACID HOSPIRA (CAP) - EMEA/H/C/002365/R/0026 (without RMP)

Applicant: Hospira UK Limited

PRAC Rapporteur: Doris Stenver

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

9.1.1. Risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders connected with human centrally authorised products

Scope: Pharmacovigilance inspection programme 2017-2020 (first revision for 2017)

Action: For adoption

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. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0063

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: PRAC consultation on a type II variation to update section 5.1 of the SmPC in order to provide information on the clinical study data experience in patients in treatment transition from an oral bisphosphonate to desunomab, information resulting from the assessment of study report 20110153 and a discussion on the issue of long term antiresorptive treatment, in particular when long-term bisphosphonate treatment is followed by denosumab

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

Disclosure of 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

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC Brexit ancillary working group

PRAC lead: Almath Spooner

Action: For discussion

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

PRAC lead: Martin Huber, Menno van der Elst, Tatiana Magalova, Albert van der Zeijden, Marianne Lunzer, Jan Neuhauser, Ulla Wändel Liminga

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh

12.2.1. Joint Paediatric Committee (PDCO)-PRAC Working Group - Guideline on conduct of pharmacovigilance for medicines used by the paediatric population – draft good pharmacovigilance practice (GVP) chapter for special populations

Action: For adoption

12.2.2. Guideline on safety and efficacy follow-up – risk management plan of advanced therapy medicinal products (ATMP) – update

PRAC lead: Brigitte Keller-Stanislawski, Julie Williams

Action: For adoption

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

12.3.1. Blood Products Working Party (BPWP) - Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products – revision

PRAC lead: Brigitte Keller-Stanislawski

Action: For discussion

12.3.2. Blood Products Working Party (BPWP) - Guideline on core SmPC for human plasma-derived and recombinant coagulation factor VIII products – revision

PRAC lead: Brigitte Keller-Stanislawski

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. European Network Training Centre (EU NTC) - operation of pharmacovigilance in the EU training needs and priorities

PRAC lead: Dolores Montero Corominas

Action: For adoption

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

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. Good Pharmacovigilance Practice (GVP) module VI on Management and reporting of adverse reactions to medicinal products - revision 2

Action: For discussion

12.12.2. Management and reporting of adverse reactions to medicinal products

None

12.12.3. Additional monitoring

None

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

Action: For information

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality - EudraVigilance auditable requirement project – update

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Good Pharmacovigilance Practices (GVP) - revised PRAC process for GVP modules in 2017 - update on GVP status overview

Action: For discussion

12.20.2. Strategy on measuring the impact of pharmacovigilance - pilot report on prioritisation of collaborative impact research topics and criteria checklist

PRAC lead: Marieke De Bruin

Action: For discussion

13. Any other business

14. Explanatory notes

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

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

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

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

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.
The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.
The evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the Package Leaflet.

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

The RMP describes what is known and not known about the side effects of a medicine and states how these risks will be prevented or minimised in patients. It also includes plans for studies and other activities to gain more knowledge about the safety of the medicine and risk factors for developing side effects.
RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available.

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

A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.
PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

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

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

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

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

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