6 February 2017
EMA/PRAC/35833/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 6-9 February 2017

Chair: June Raine – Vice-Chair: Almath Spooner

06 February 2017, 13:00 – 19:30, room 3/A

07 February 2017, 08:30 – 19:30, room 3/A

08 February 2017, 08:30 – 19:30, room 3/A

09 February 2017, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

23 February 2017, 09:00 – 12:00, room 7/B, via teleconference

Health and safety information

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

Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scope 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 February 2017. See February 2017 PRAC minutes (to be published post March 2017 PRAC meeting).

1.2. Adoption of agenda of the meeting of 6-9 February 2017

Action: For adoption

1.3. Adoption of the minutes of the previous meeting of 9-12 January 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

3.1.1. 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: To be appointed; PRAC Co-rapporteur: To be appointed

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 adoption of a list of questions

3.2. Ongoing procedures

3.2.1. 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); moroctocog alfa – REFACTO AF (CAP) octocog alfa – ADVATE (CAP), HELIXATE NEXGEN (CAP), IBLIAS (CAP), KOGENATE (CAP), KOVALTRY (CAP) - EMEA/H/A-31/1448

Applicant: Baxter AG (Advate), Bayer Pharma AG (Helixate Nexgen, Iblias, Kogenate, Kovaltry), CSL Behring GmbH (Voncento), Pfizer Limited (Refacto AF), various

PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Brigitte Keller-Stanislawski

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

Action: For adoption of a list of experts for the ad hoc expert group meeting

3.2.2. Paracetamol[1] (NAP) - EMEA/H/A-31/1445

Applicant: GlaxoSmithKline Consumer Healthcare AB (Alvedon, 665 mg modified-release tablet), various

PRAC Rapporteur: Laurence de Fays; PRAC Co-rapporteur: Ulla Wändel Liminga

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

[1] Modified release formulations

Action: For adoption of a list of experts for the ad hoc expert group meeting

3.3. Procedures for finalisation

3.3.1. Sodium-glucose co-transporter 2 (SGLT2) inhibitors: Canaglifozin – INVOKANA (CAP); canagliflozin, metformin – VOKANAMET (CAP); dapaglifozin – EDISTRIDE (CAP), FORXIGA (CAP); dapaglifozin, metformin – XIGDUO (CAP), EBYMECT (CAP); empaglifozin – JARDIANCE (CAP); empaglifozin, metformin – SYNJARDY (CAP) - EMEA/H/A-20/1442

Applicant: Janssen-Cilag International N.V. (Invokana, Vokanamet); AstraZeneca AB (Edistride, Forxiga, Xigduo, Ebymect); Boehringer Ingelheim International GmbH (Jardiance; Synjardy)

PRAC Rapporteur: Valerie Strassmann; PRAC Co-rapporteur: Menno van der Elst

Scope: Review of the benefit-risk balance of sodium-glucose co-transporter-2 (SGLT2) inhibitors following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004, based on pharmacovigilance data

Action: For adoption of a recommendation to CHMP

3.4. Article 5(3) of Regulation (EC) No 726/2004 as amended: PRAC advice on CHMP request

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

None

4.2. New signals detected from other sources

4.2.1. Dabigatran – PRADAXA (CAP); lovastatin (NAP); simvastatin (NAP)

Applicant: Boehringer Ingelheim International GmbH (Pradaxa), various

PRAC Rapporteur: To be appointed

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

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

Action: For adoption of PRAC recommendation

EPITT 18819 – New signal

Lead Member State: DK

4.2.2. Darbepoetin alfa – ARANESP (CAP); epoetin alfa – ABSEAMED (CAP), BINOCRIT (CAP), EPOETIN ALFA HEXAL (CAP), NAP; epoetin beta – NEORECORMON (CAP); epoetin theta – BIOPOIN (CAP), EPORATIO (CAP); epoetin zeta – RETACRIT (CAP), SILAPO (CAP), Methoxy polyethylene glycol-epoetin beta – MIRCERA (CAP); NAPs

Applicants: Amgen Europe B.V. (Aranesp), Hexal AG (Epoetin Alfa Hexal), Hospira UK Limited (Retacrit), Medice Arzneimittel Pütter GmbH & Co. KG (Abseamed), Roche Registration Limited (Neorecormon, Mircera), Ratiopharm GmbH (Eporatio), Sandoz GmbH (Binocrit), Stada Arzneimittel AG (Silapo), Teva GmbH (Biopoin); various

PRAC Rapporteur: To be appointed

Scope: Signal of severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)

Action: For adoption of PRAC recommendation

EPITT 18846 – New signal

Lead Member State: DE

4.2.3. Levonorgestrel[3] (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

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

Action: For adoption of PRAC recommendation

EPITT 18849 – New signal

Lead Member State: DE

4.2.4. Selexipag - UPTRAVI (CAP)

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Rafe Suvarna

Scope: Signal of fatal cases in patients with pulmonary arterial hypertension (PAH)

Action: For adoption of PRAC recommendation

EPITT 18833 – New signal

Lead Member State: UK

[3] Intrauterine device (IUD)

4.2.5. Tick-borne encephalitis vaccine (inactivated) (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of potential vaccination failure in children

Action: For adoption of PRAC recommendation

EPITT 18825– New signal

Lead Member State: DE

4.3. Signals follow-up and prioritisation

4.3.1. Dexlansoprazole (NAP); lansoprazole (NAP)

Applicant: various

PRAC Rapporteur: Kirsti Villikka

Scope: Signal of unexpected histopathological findings from a juvenile rat toxicity study

Action: For adoption of PRAC recommendation

EPITT 18645 – Follow-up to October 2016

4.3.2. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/SDA/023; BYETTA (CAP) - EMEA/H/C/000698/SDA/043

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of incorrect use of device associated with (serious) adverse reactions including hyperglycaemia and hypoglycaemia

Action: For adoption of PRAC recommendation

EPITT 18688 – Follow-up to July 2016

4.3.3. Fluconazole (NAP)

Applicant: various

PRAC Rapporteur: Doris Stenver

Scope: Signal of spontaneous abortion and stillbirth

Action: For adoption of PRAC recommendation

EPITT 18666 – Follow-up to January 2016

4.3.4. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/SDA/014

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of pemphigoid

Action: For adoption of PRAC recommendation

EPITT 18759 – Follow-up to October 2016

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Carglumic acid - EMEA/H/C/004019

Scope: Treatment of hyperammoniemia

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

5.1.2. Cariprazine - EMEA/H/C/002770

Scope: Treatment of schizophrenia

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

5.1.3. Cenegermin - EMEA/H/C/004209, Orphan

Applicant: Dompe Farmaceutici S.p.A.

Scope, accelerated assessment: Treatment of neurotrophic keratitis

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

5.1.4. Dimethyl fumarate - EMEA/H/C/002157

Scope: Treatment of moderate to severe plaque psoriasis in adults in need of systemic drug therapy, treatment of plaque psoriasis

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

5.1.5. Emtricitabine, tenofovir disoproxil –EMEA/H/C/004686

Scope: Treatment of human immunodeficiency virus (HIV)-1 infection

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

5.1.6. Etanercept - EMEA/H/C/004192

Scope: Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis, plaque psoriasis and paediatric plaque psoriasis

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

5.1.7. Expanded human allogeneic mesenchymal adult - EMEA/H/C/004258

ATMP[4]

Scope: Treatment of complex perianal fistula(s)

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

5.1.8. Febuxostat - EMEA/H/C/004374

Scope: Treatment of hyperuricaemia

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

5.1.9. Iloperidone - EMEA/H/C/004149

Scope: Treatment of schizophrenia

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

5.1.10. Inotuzumab ozogamicin - EMEA/H/C/004119, Orphan

Applicant: Pfizer Limited

Scope: Treatment of B-cell precursor acute lymphoblastic leukaemia (ALL)

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

5.1.11. Masitinib - EMEA/H/C/004159, Orphan

Applicant: AB Science

Scope: Treatment of mastocytosis

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

5.1.12. Parathyroid hormone - EMEA/H/C/003861, Orphan

Applicant: NPS Pharma Holdings Limited

Scope: Treatment of hypoparathyroidism

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

5.1.13. Patiromer sorbitex calcium - EMEA/H/C/004180

Scope: Treatment of hyperkalaemia

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

[4] Advanced therapy medicinal product

5.1.14. Rituximab - EMEA/H/C/003903

Scope: Treatment of non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL), rheumatoid arthritis and granulomatosis with polyangiitis and microscopic polyangiitis

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

5.1.15. Rituximab - EMEA/H/C/004729

Scope: Treatment of non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL), rheumatoid arthritis and granulomatosis with polyangiitis and microscopic polyangiitis

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

5.1.16. Sarilumab - EMEA/H/C/004254

Scope: Treatment of active rheumatoid arthritis

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

5.1.17. Spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736

ATMP[5]

Scope: Treatment of cartilage defects

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

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

5.2.1. Albiglutide - EPERZAN (CAP) - EMEA/H/C/002735/II/0028/G

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: Grouped variation to update the RMP in order to: 1) introduce additional risk minimisation measures addressing the important potential risk of medication errors. Annex II of the product information is updated accordingly; 2) add a new category 3 study as an additional pharmacovigilance activity: study 204879: a randomized, open-label, active-controlled, parallel-group, exploratory study on the effects of repeated doses of albiglutide compared to exenatide on gastric myoelectrical activity and gastric emptying in subjects with type 2 diabetes mellitus (T2DM); 3) add a new category 3 study as an additional pharmacovigilance activity – study 201840: an exploratory randomized, 2-part, single-blind, 2-period crossover study comparing the effect of albiglutide with exenatide on regional brain activity related to nausea in healthy volunteers; 4) add a new category 3 study as an additional pharmacovigilance activity: cross-sectional survey to assess the effectiveness of the proposed additional educational materials using patient connect

[5] Advance therapy medicinal product

Action: For adoption of PRAC Assessment Report

5.2.2. Antithrombin alfa - ATRYN (CAP) - EMEA/H/C/000587/II/0027

Applicant: GTC Biotherapeutics UK Limited

PRAC Rapporteur: Claire Ferard

Scope: Introduction of a RMP (version 1) as requested in the sixth annual re-assessment (EMEA/H/C/000587/S/0021) and second five-year renewal (EMEA/H/C/000587/R/0024)

Action: For adoption of PRAC Assessment Report

5.2.3. Eribulin - HALAVEN (CAP) - EMEA/H/C/002084/II/0033

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 4.2) following the revision of the protocol for a post-authorisation study (PAS) to capture data on the frequency of resolution and time to resolution of eribulin-induced or aggravated peripheral neuropathy from a phase 3 study, E7389-A001-303 (ACCRU: a randomized phase III trial of eribulin compared to standard weekly paclitaxel as first- or second-line therapy for locally recurrent or metastatic breast cancer) to an observational post authorisation, single-arm, prospective multicentre cohort study E7389-M044-504 (IRENE). The submission of the corresponding study report to the EMA/PRAC remains unchanged and is planned in 2019

Action: For adoption of PRAC Assessment Report

5.2.4. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0042

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP (version 25) following closure and final summary of the exenatide pregnancy registry (a prospective, observational study conducted in the United States that actively collected information on exposure to antidiabetic medication during pregnancy and the associated pregnancy outcomes in patients with type 2 diabetes mellitus (T2CM)). Moreover, the MAH included additional minor updates to the RMP

Action: For adoption of PRAC Assessment Report

5.2.5. Retigabine - TROBALT (CAP) - EMEA/H/C/001245/II/0045

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

Scope: Update of the RMP (version 18) in order to remove a post-authorisation study (PASS) RTG116158: an open label study evaluating the effects of retigabine added to existing anti-epileptic drug(s) on urinary voiding function in subjects with partial onset seizures

Action: For adoption of PRAC Assessment Report

5.2.6. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/II/0014, Orphan

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 6.1) in order to add off-label use in patients with idiopathic pulmonary pneumonia, with or without pulmonary hypertension as an important identified risk

Action: For adoption of PRAC Assessment Report

5.2.7. Thyrotropin alfa - THYROGEN (CAP) - EMEA/H/C/000220/II/0088

Applicant: Genzyme Europe BV

PRAC Rapporteur: Almath Spooner

Scope: Update of the RMP (version 9.0) to bring it in line with the latest RMP template. As a consequence, 'gastrointestinal symptoms', 'constitutional symptoms' and 'injection site reactions' are deleted resulting from their downgrade to identified risks as not categorized as important any longer. In addition, 'perceived lower thyroid-stimulating hormone (TSH) elevation after thyrotropin alfa administration' is deleted from the list of important potential risks as it does not correspond to a safety risk for patients treated with Thyrogen. Finally, the study results and completion date for the T4 study (collection of data about remnant ablation in patients originally diagnosed with T4 thyroid cancer) are added and as a consequence, use of Thyrogen for remnant ablation in patients originally diagnosed with T4N0-1M0-1 thyroid cancer' is removed as missing information

Action: For adoption of PRAC Assessment Report

5.2.8. Vildagliptin - GALVUS (CAP) - EMEA/H/C/000771/WS1088/0048; JALRA (CAP) - EMEA/H/C/001048/WS1088/0048; XILIARX (CAP) - EMEA/H/C/001051/WS1088/0047 Vildagliptin, metformin hydrochloride - EUCREAS (CAP) - EMEA/H/C/000807/WS1088/0057; ICANDRA (CAP) - EMEA/H/C/001050/WS1088/0058; ZOMARIST (CAP) - EMEA/H/C/001049/WS1088/0058

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMPs for Galvus, Jalra, Xiliarx, Eucreas, Icandra and Zomarist in order to reflect the outcome of the recently finalised procedure for metformin-containing products under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1432) in order to implement a targeted questionnaire for cases of lactic acidosis

Action: For adoption of PRAC Assessment Report

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

5.3.1. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0038

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC following the completion of the post-authorisation efficacy studies: IM103-008 (belatacept evaluation of nephro-protection and efficacy as first-line immunosuppression trial (BENEFIT) and IM103-027 (belatacept evaluation of nephro-protection and efficacy as first-line immunosuppression trial - extended criteria donors (BENEFIT-EXT)). 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

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

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped application including: 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

5.3.3. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0043, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to add data from study C25007: a single-arm study of brentuximab vedotin in patients with relapsed or refractory Hodgkin lymphoma who are not suitable for stem cell transplantation or multi-agent chemotherapy. The submission of the clinical study report fulfils SOB 011 of the conditional marketing authorisation for Adcetris. The RMP (version 8.0) is updated accordingly

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

5.3.4. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0002, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to add the treatment of adult patients with multiple myeloma who have received at least one prior therapy. As a consequence, sections 4.2, 4.4, 4.5, 5.1

and 5.2 of the SmPC are updated. A new warning is introduced in section 4.4 regarding neutropenia/thrombocytopenia induced by background therapy. Annex II is also updated to remove all the specific obligations following submissions of the final results of studies MMY3003 (a phase III randomised study investigating lenalidomide and dexamethasone with or without daratumumab in patients with previously treated multiple myeloma) and MMY3004 (a phase III randomised study investigating bortezomib and dexamethasone with or without daratumumab in patients with previously treated multiple myeloma). The Package Leaflet and RMP (version 2) 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

5.3.5. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/X/0054, Orphan

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

5.3.6. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0035

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to include 'liver function abnormalities' as an adverse event observed in the post-marketing setting and to clarify events not observed in placebo-controlled studies. The Package Leaflet and the RMP (version 8) are updated accordingly. The MAH has also taken the opportunity to make minor administrative changes in the Package Leaflet

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

5.3.7. Efmoroctocog alfa - ELOCTA (CAP) - EMEA/H/C/003964/II/0010

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Rafe Suvarna

Scope: Submission of the final clinical study report (CSR) for study 997HA307 (RMP category 3) to investigate the pharmacokinetics (PK) of recombinant Factor VIII Fc fusion protein (rFVIIIFc) at two vial strengths (1000 and 3000IU) and evaluate the safety of rFVIIIFc. The RMP (version 1.5) is updated accordingly

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

5.3.8. 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

5.3.9. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/II/0131

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to include treatment of human immunodeficiency virus (HIV)-1 infected adolescents, with nucleoside reverse transcriptase inhibitors (NRTI) resistance or toxicities precluding the use of first line agents, aged 12 to <18 years for Truvada. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 13) are updated accordingly

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

5.3.10. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP) - EMEA/H/C/002673/WS0992/0022/G;REVINTY ELLIPTA (CAP) - EMEA/H/C/002745/WS0992/0017/G

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Grouped variations to update sections 4.4, 4.8 and 5.1 of the SmPC in order to include data from study HZC113782 (SUMMIT): clinical outcomes study comparing the effect of fluticasone furoate/vilanterol inhalation powder 100/25mcg with placebo on survival in subjects with moderate chronic obstructive pulmonary disease (COPD) and a history of or at increased risk for cardiovascular disease. In addition, section 4.8 of the SmPC is updated to add 'paradoxical bronchospasm' to the list of adverse reactions as well as section 5.1 of the SmPC to correct an error identified in the pharmacodynamic section. The Package Leaflet, Labelling and RMP (version 8.1) are updated accordingly

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

5.3.11. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP) - EMEA/H/C/002673/WS1101/0029; REVINTY ELLIPTA (CAP) - EMEA/H/C/002745/WS1101/0025

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of section 5.1 of the SmPC in order to update the safety information with the results of HZC115151 study: a 12-month, open label, randomised, effectiveness study to evaluate fluticasone furoate/vilanterol inhalation powder delivered once daily via a novel dry powder inhaler (NDPI) compared with the existing chronic obstructive pulmonary disease (COPD) maintenance therapy alone in subjects with COPD (Annex II condition) of the Relvar Ellipta and Revinty Ellipta (92/22mcg strength only). The RMP (version 8.3) is updated accordingly

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

5.3.12. 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

5.3.13. Gefitinib - IRESSA (CAP) - EMEA/H/C/001016/II/0026

Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final study report for the IMPRESS study (D791LC00001): a phase III randomised, double blind, placebo controlled, parallel, multicentre study to assess the efficacy and safety of continuing Iressa 250 mg in addition to chemotherapy versus chemotherapy alone in patients who have epidermal growth factor receptor (EGFR) mutation positive locally advanced or metastatic non-small cell lung cancer (NSCLC) and have progressed on first line Iressa. In addition, the procedure includes a discussion in line with the conclusions of PSUSA procedure (EMEA/H/C/PSUSA/00001518/201507) concluded in January 2016. No change to the Product Information and RMP is proposed

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

5.3.14. Human fibrinogen, human thrombin - EVARREST (CAP) - EMEA/H/C/002515/II/0027/G

Applicant: Omrix Biopharmaceuticals N. V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) submission of the final results for study BIOS-13-005 (a phase III, randomized, controlled, superiority study evaluating Evarrest fibrin sealant patch versus standard of care treatment in controlling parenchymal bleeding during hepatic surgery) updating the efficacy and safety information; 2) submission of the final results for study BIOS-13-004 (a single-blinded, randomized, controlled, comparative phase III study evaluating the safety and effectiveness of Evarrest fibrin sealant patch as an adjunct to haemostasis during cardiovascular surgery) updating the efficacy and safety information; 3) submission of the final results for study 400-12-002 (a randomized, controlled, comparative phase II study evaluating the safety and effectiveness of Evarrest fibrin sealant patch as an adjunct to haemostasis during cardiovascular surgery) updating the efficacy and safety information; 4) submission of the final results for study 400-12-005 (a non-investigational post-market trial using Evarrest fibrin sealant patch as an adjunct to

haemostasis in soft tissue bleeding during intra-abdominal, retroperitoneal, pelvic and non-cardiac thoracic surgery) updating the safety information; 5) update of section 5.1 of the SmPC to include further information on main existing efficacy studies. As a consequence, sections 4.8, 5.1 of the SmPC are also updated. In addition, the product information (PI) is brought in line with the latest QRD template (version 10) and Guideline on core SmPC for plasma-derived fibrin/sealant/haemostatic products (EMA/CHMP/BPWP/598816/2010 rev.1). Furthermore, section 4.2 is updated regarding the paediatric information for children under the age of 1 month, according to the EMA waiver. The RMP (version 3) is updated accordingly, including consequential and routine changes

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

5.3.15. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0025, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Update of section 4.4 of the SmPC to remove the warning and precaution regarding the effect of ibrutinib on the QT interval and section 5.1 to provide additional information regarding the pharmacodynamic effect of ibrutinib on QT/QTc intervals and cardiac electrophysiology. The RMP (version 6.1) is updated accordingly

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

5.3.16. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/II/0003, Orphan

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Extension of indication to include treatment of patients with Duchenne muscular dystrophy in whom respiratory function has started to decline and who are currently not taking concomitant glucocorticoids. The RMP (version 2.0) is updated accordingly

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

5.3.17. 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 'potential risk of malignant neoplasms following combination treatment with insulin detemir + liraglutide + metformin'

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

5.3.18. 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 to provide additional information on the breast cancer cases found in LEADER (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

5.3.19. 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

5.3.20. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/II/0017

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data from study VX12 809 105: a phase III, rollover study to evaluate the safety and efficacy of long term treatment with lumacaftor/ivacaftor in subjects aged 12 years and older with cystic fibrosis, homozygous or heterozygous for the F508del cystic fibrosis transmembrane conductance regulator (CFTR) mutation (MEA 001). The RMP (version 2.7) is updated accordingly. In addition, the MAH took the opportunity to bring the Product Information in line with the latest QRD template (version 10)

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

5.3.21. Maraviroc - CELSENTRI (CAP) - EMEA/H/C/000811/X/0046/G

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Line extension to introduce a new pharmaceutical form (20mg/ml oral solution) and two new strengths of film-coated tablets (25mg and 75mg) to the currently approved presentations for Celsentri, grouped with an extension of indication to include paediatric use (2 to 18 years). As a consequence, sections 4.2 and 4.4 of the SmPC are updated to detail posology in paediatric patients and to update the safety information respectively. The Package Leaflet, Labelling and RMP (version 11) 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

5.3.22. 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

5.3.23. Peginterferon alfa-2a - PEGASYS (CAP) - EMEA/H/C/000395/II/0091

Applicant: Roche Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to include paediatric patients from 3 to less than 18 years of age with chronic hepatitis B in the immune-active phase for Pegasys. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add efficacy and safety information from study YV25718: a Phase IIIb parallel group, open label study of pegylated interferon alfa-2a monotherapy compared to untreated control in children with HBeAg positive chronic hepatitis B. 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

5.3.24. Pirfenidone - ESBRIET (CAP) - EMEA/H/C/002154/X/0035/G, Orphan

Applicant: Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Line extension to introduce a new pharmaceutical form associated with 3 new strengths (267 mg, 534 mg and 801 mg film-coated tablets). In addition, manufacturing sites are also introduced for the currently approved 267mg hard capsules presentations (EU/1/11/667/001-003). The RMP (version 8.0) is updated accordingly

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

5.3.25. Pertuzumab - PERJETA (CAP) - EMEA/H/C/002547/II/0028

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Final clinical study report for the TRYPHAENA study (BO22280): a randomised, multicentre, multinational phase II study to evaluate pertuzumab in combination with trastuzumab, given either concomitantly or sequentially with standard anthracycline based chemotherapy or concomitantly with a non-anthracycline-based chemotherapy regimen, as neoadjuvant therapy for patients with locally advanced, inflammatory or early stage HER2-positive breast cancer. The RMP (version 8) is updated accordingly

Action: For adoption of PRAC Assessment Report

5.3.26. 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

5.3.27. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/II/0036

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Extension of indication to add the treatment of chronic hepatitis C in adolescents aged 12 to <18 years. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add information on posology, warnings, safety, efficacy and pharmacokinetics. The Package Leaflet and the RMP (version 5.0) 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

5.3.28. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/II/0003

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.4, 4.5 and 5.1 of the SmPC in order to reflect on emerging clinical data from study GS-US-342-1202 (a phase III, open-label study to investigate the efficacy and safety of sofosbuvir/velpatasvir fixed dose combination for 12 weeks in subjects with chronic hepatitis C virus (HCV) and human immunodeficiency virus (HIV)-1

coinfection). The RMP (version 1.0) is updated accordingly. In addition, minor administrative changes are implemented throughout the Product Information

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

5.3.29. Trametinib - MEKINIST (CAP) - EMEA/H/C/002643/WS0996/0018; Dabrafenib - TAFINLAR (CAP) - EMEA/H/C/002604/WS0996/0022

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the combination treatment with trametinib and dabrafenib of adult patients with advanced non-small cell lung cancer (NSCLC) with a BRAF V600 mutation. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the Mekinist and Tafinlar SmPC are updated. The Package Leaflet and RMPs are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to align the SmPCs of Mekinist and Tafinlar. 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

5.3.30. Temsirolimus - TORISEL (CAP) - EMEA/H/C/000799/II/0063, Orphan

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Final results from study 3066K1-4438-WW (B1771007) entitled 'a randomized phase 4 study comparing two intravenous temsirolimus (TEMSR) regimens in subjects with relapsed, refractory mantle cell lymphoma' and fulfilment of obligation to conduct post authorisation measure ANX 027.2. In addition, submission of the toxic effects of interest (e.g. bleeding, infection- and mucositis-related events) for study 3066K1-4438-WW (post-marketing commitment MEA 028) together with a review discussing potential new safety concerns arising from the results. The RMP (version 3.0) is updated accordingly to add myocardial infarction and cardiovascular events in patient with coexisting cardiovascular conditions as important potential risks, and anaemia, thrombocytopenia, hypercholesterolemia, and hypertriglyceridemia as important identified risks. Furthermore, 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

5.3.31. Vismodegib - ERIVEDGE (CAP) - EMEA/H/C/002602/II/0032

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 5.3 of the SmPC in order to reflect non-clinical carcinogenicity studies (MEA 003): 1) study 13-0322: a 26-week oral gavage carcinogenicity study with vismodegib in hemizygous CByB6F1-Tg(HRAS)2Jic mice; 2) study 13-0323: a 104-week and 52-week with a 12-week recovery phase oral gavage carcinogenicity study with vismodegib in Sprague Dawley rats. The RMP (version 12.0) is updated accordingly. Furthermore,

additional routine changes (including some resulting from the assessment of RMP version 11) have been introduced

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 - BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP) - PSUSA/00009005/201607

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Aflibercept[6] - ZALTRAP (CAP) - PSUSA/00010019/201608 (with RMP)

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Antithrombin alpha - ATRYN (CAP) - PSUSA/00000224/201607

Applicant: GTC Biotherapeutics UK Limited

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Asparaginase[7] - SPECTRILA (CAP) - PSUSA/00010445/201607

Applicant: Medac Gesellschaft fur klinische Spezialpraparate GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[6] Oncology indication(s) only
[7] Centrally authorised product(s) only

6.1.5. Ataluren - TRANSLARNA (CAP) - PSUSA/00010274/201607

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Atazanavir, cobicistat - EVOTAZ (CAP) - PSUSA/00010404/201607 (with RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Birch bark extract[8] - EPISALVAN (CAP) - PSUSA/00010446/201607

Applicant: Birken AG

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Brivaracetam - BRIVIACT (CAP) - PSUSA/00010447/201607

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/201607

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Catridecacog - NOVOTHIRTEEN (CAP) - PSUSA/00010034/201607

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Claire Ferard

[8] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

6.1.11. Dapagliflozin, metformin - EBYMECT (CAP); XIGDUO (CAP) - PSUSA/00010294/201607

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Dasabuvir - EXVIERA (CAP) - PSUSA/00010363/201607

Applicant: AbbVie Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Dolutegravir – TIVICAY (CAP); dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - PSUSA/00010075/201607

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Etanercept[9] - BENEPALI (CAP) - PSUSA/00010452/201607

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Evolocumab - REPATHA (CAP) - PSUSA/00010405/201607

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] Etanercept - Benepali centrally authorised product only

6.1.16. Idursulfase - ELAPRASE (CAP) - PSUSA/00001722/201607

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Icatibant - FIRAZYR (CAP) - PSUSA/00001714/201607

Applicant: Shire Orphan Therapies GmbH

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Idelalisib - ZYDELIG (CAP) - PSUSA/00010303/201607

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Ingenol mebutate - PICATO (CAP) - PSUSA/00010035/201607

Applicant: Leo Pharma A/S

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Lipegfilgrastim - LONQUEX (CAP) - PSUSA/00010111/201607

Applicant: Sicor Biotech UAB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Lomitapide - LOJUXTA (CAP) - PSUSA/00010112/201607

Applicant: Aegerion Pharmaceuticals Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Modified vaccinia Ankara virus - IMVANEX (CAP) - PSUSA/00010119/201607

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ombitasvir, paritaprevir , ritonavir - VIEKIRAX (CAP) - PSUSA/00010367/201607

Applicant: AbbVie Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Pegaspargase[10] - ONCASPAR (CAP) - PSUSA/00010457/201607

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Peginterferon beta-1A - PLEGRIDY (CAP) - PSUSA/00010275/201607

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Perampanel - FYCOMPA (CAP) - PSUSA/00009255/201607

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Phenylephrine, ketorolac - OMIDRIA (CAP) - PSUSA/00010419/201607

Applicant: Omeros London Limited

[10] Centrally authorised product(s) only

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Romiplostim - NPLATE (CAP) - PSUSA/00002660/201607

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Rotavirus vaccine monovalent (live, oral) - ROTARIX (CAP) - PSUSA/00002665/201607

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Simoctocog alfa - NUWIQ (CAP) - PSUSA/00010276/201607

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Stavudine - ZERIT (CAP) - PSUSA/00002787/201606 (with RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Tocofersolan - VEDROP (CAP) - PSUSA/00002981/201607

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

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Vorapaxar - ZONTIVITY (CAP) - PSUSA/00010357/201607

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Carmela Macchiarulo

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. Aripiprazole - ABILIFY (CAP); ABILIFY MAINTENA (CAP); ARIPIPRAZOLE SANDOZ (CAP); NAP - PSUSA/00000234/201607

Applicant: Otsuka Pharmaceutical Europe Ltd (Abilify, Abilify Maintena), Sandoz GmbH (Aripiprazole Sandoz), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Nitric oxide - INOMAX (CAP); NAP - PSUSA/00002172/201606

Applicant: Linde Healthcare AB (INOmax), various

PRAC Rapporteur: Julie Williams

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. Dienogest, estradiol[11] (NAP)- PSUSA/00010443/201606

Applicant: various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Ganciclovir (NAP) - PSUSA/00001516/201606

Applicant: various

PRAC Lead: Sabine Straus

[11] Hormone replacement therapy (HRT) indication(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Ibuprofen, pseudoephedrine (NAP) - PSUSA/00001711/201607

Applicant: various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Levonorgestrel, ethinylestradiol; ethinylestradiol[12] (NAP) - PSUSA/00010442/201607

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Midodrine (NAP) - PSUSA/00003178/201606

Applicant: various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Misoprostol[13] (NAP) - PSUSA/00010291/201606

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Trastuzumab - HERCEPTIN (CAP) - EMEA/H/C/000278/LEG 098.1

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to LEG 098 [submission of a proposal for a DHPC to treating

[12] Combination pack
[13] Gastrointestinal indication(s) only

oncologists and/or oncologists to ensure awareness of the need to follow the current guidance on cardiac monitoring during and after completion of treatment with Herceptin and to highlight the need for cardiac monitoring during handover of patient management to other physicians as requested in the conclusions of EMEA/H/C/PSUSA/00003010/201509 adopted in April 2016] as per the request for supplementary information (RSI) adopted by PRAC in October 2016

Action: For adoption of advice to CHMP

6.4.2. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/LEG 017

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a detailed review on arterial and venous thromboembolic events (ATE/VTE) including a discussion on the biological plausibility based on the mechanism of action of ulipristal acetate, focusing on the role of oestrogen and progesterone as requested in the conclusions of PSUSA/00009325/201602 adopted by PRAC and CHMP in September 2016

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[14]

7.1.1. Cidofovir (NAP) - EMEA/H/N/PSP/S/0052

Applicant: Emcure Pharma UK Ltd (Cidofovir Emcure Pharma)

PRAC Rapporteur: Julie Williams

Scope: Protocol (version 1.0) for a non-interventional, prospective, exposure (safety outcome) registry study of cidofovir to further elucidate the characteristics of the different patient populations for cidofovir use, gather details of adverse events and patient outcome following treatment in a specified indication

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

7.1.2. Ferric citrate coordination complex - FEXERIC (CAP) - EMEA/H/C/003776/PSP/S/0038.1

Applicant: Keryx Biopharma UK Ltd.

PRAC Rapporteur: Julie Williams

Scope: Revised protocol (KRX-0502-401, version 1.0) for an imposed non-interventional observational post-authorisation study to assess the safety of Fexeric as a phosphate binder in routine clinical practice as per the conclusions of procedure EMEA/H/C/PSP/0038 adopted

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

by PRAC in March 2016

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

7.1.3. Ethinylestradiol (NAP); levonorgestrel, ethinylestradiol (NAP); - EMEA/H/C/PSP/0037.2

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Claire Ferard

Scope: Revised protocol (version 5.0) for an imposed non-interventional post-authorisation study to assess the risk of venous thromboembolic events (VTE) in women exposed to Seasonique as per the conclusion of the procedure EMEA/H/C/PSP/0037.1 adopted by PRAC in September 2016

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

7.1.4. Roflumilast - DALIRESP (CAP); DAXAS (CAP); LIBERTEK (CAP) - EMEA/H/C/PSA/J/0014

Applicant: AstraZeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: Revised protocol following substantial amendments to the previously agreed protocol in October 2011 by CHMP for a PASS study (D7120R00003, previously RO-2455-403-RD): a long-term comparative observational safety study to evaluate mortality rate, including cardiovascular, suicide and cancer death rates and incidence rate of hospitalisations in treated chronic obstructive pulmonary disease (COPD) patients compared to match COPD patients not treated with roflumilast

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

7.1.5. Teicoplanin (NAP) EMEA/H/C/PSA/S/0013

Applicant: Sanofi-aventis (Targocid)

PRAC Rapporteur: Valerie Strassmann

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

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[15]

7.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 006.2

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: MAH's response to MEA 06.1 [Submission of a revised protocol for a pregnancy registry study OBS13436: an international Lemtrada pregnancy exposure cohort in multiple sclerosis] as per the request for supplementary information (RSI) adopted by PRAC in September 2016

Action: For adoption of advice to CHMP

7.2.2. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 017.1

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 017 [PASS protocol for study ALIROC07997: 'monitoring of the safety of alirocumab in human immunodeficiency virus (HIV)-infected patients, using healthcare databases'] as per the request for supplementary information (RSI) adopted by PRAC in November 2016

Action: For adoption of advice to CHMP

7.2.3. Collagenase clostridium histolyticum - XIAPEX (CAP) - EMEA/H/C/002048/MEA 030

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Protocol for study Sobi.Xiapex-PASS02: a non-interventional post-authorisation safety study (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)

Action: For adoption of advice to CHMP

7.2.4. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 003.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's responses to MEA 003: revised PASS protocol to evaluate the incidence of diabetic ketoacidosis (DKA) in sodium-dependent glucose cotransporters (SGLT)-2 inhibitors as an outcome of the Article 20 referral on sodium-dependent glucose cotransporters (SGLT)-2 inhibitors (EMEA/H/A-20/1419), as per request for supplementary information (RSI) adopted in September 2016

[15] 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

Action: For adoption of advice to CHMP

7.2.5. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/MEA 020.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's responses to MEA 020: revised PASS protocol to evaluate the incidence of diabetic ketoacidosis (DKA) in sodium-dependent glucose cotransporters (SGLT)-2 inhibitors as an outcome of the Article 20 referral on sodium-dependent glucose cotransporters (SGLT)-2 inhibitors (EMEA/H/A-20/1419), as per request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.2.6. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/MEA 003.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 003: revised PASS protocol to evaluate the incidence of diabetic ketoacidosis (DKA) in sodium-dependent glucose cotransporters (SGLT)-2-inhibitors as an outcome of the Article 20 referral on SGLT-2 inhibitors (EMEA/H/A-20/1419), as per request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.2.7. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 006.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 006: revised PASS protocol to evaluate the incidence of diabetic ketoacidosis (DKA) in sodium-dependent glucose cotransporters (SGLT)-2-inhibitors as an outcome of the Article 20 referral on SGLT-2 inhibitors (EMEA/H/A-20/1419), as per request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.2.8. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/MEA 034.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Revised protocol (version 02) for study CENA713D2409: a drug utilisation study (DUS) in patients treated with Exelon/Prometax (rivastigmine) transdermal patch, as per the request for supplementary information (RSI) adopted in April 2014

Action: For adoption of advice to CHMP

7.2.9. Rivastigmine - PROMETAX (CAP) - EMEA/H/C/000255/MEA 035.1

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Revised protocol (version 02) for study CENA713D2409: a drug utilisation study (DUS) in patients treated with Exelon/Prometax (rivastigmine) transdermal patch, as per the request for supplementary information (RSI) adopted in April 2014

Action: For adoption of advice to CHMP

7.2.10. Safinamide - XADAGO (CAP) - EMEA/H/C/002396/MEA 004.2

Applicant: Zambon SpA

PRAC Rapporteur: Almath Spooner

Scope: Scope: MAH's response to MEA 004.1 [revised protocol for study Z7219N02: a drug utilisation study (DUS): observational European multicentre retrospective-prospective cohort study to observe Safinamide safety profile and pattern of use in clinical practice during the first post-commercialisation phase] as per request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.2.11. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 001.1

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Rafe Suvarna

Scope: MAH’s response to MEA 001 [protocol for a non-interventional non-imposed PASS: observational cohort study of pulmonary arterial hypertension (PAH) patients exposed and unexposed to selexipag in routine clinical practice] as per request for supplementary information (RSI) adopted in October 2016

Action: For adoption of advice to CHMP

7.2.12. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 024.9

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: MAH’s response to MEA 024.8 [revised protocol (CNTO1275PSO4007) and sixth interim report for the pregnancy research initiative study] as per request for supplementary information (RSI) adopted in July 2016

Action: For adoption of advice to CHMP

7.2.13. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.2

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 044.1 [revised protocol for for an adolescent registry: an observational PASS of ustekinumab in the treatment of pediatric patients aged 12 years and older with moderate to severe plaque psoriasis] as per the request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[16]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[17]

7.4.1. Aflibercept - ZALTRAP (CAP) - EMEA/H/C/002532/II/0034

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final results of the drug utilisation study monitoring the use of Zaltrap in cancer patients including potential off-label use and evaluating the potential for intravitreal use. This fulfils the post authorisation commitment MEA 03

Action: For adoption of PRAC Assessment Report

7.4.2. 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

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

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variation including the 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

[16] In accordance with Article 107p-q of Directive 2001/83/EC
[17] 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

accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. 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. No change in the Product Information is proposed

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. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/MEA 021.3

Applicant: Bristol-Myers Squibb, Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Interim study report of study CV185-365: evaluation of the effectiveness of Eliquis (apixaban) risk minimisation tools in the European Economic Area (EEA) countries

Action: For adoption of advice to CHMP

7.5.2. Human normal immunoglobulin - PRIVIGEN (CAP) - EMEA/H/C/000831/MEA 022.5

Applicant: CSL Behring GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Second interim report for study IgPro10_5003: an observational hospital-based cohort study in the US on 'Privigen use and haemolytic anaemia in adults and children and Privigen safety profile in children with chronic inflammatory demyelinating polyneuropathy (CIDP) (as per the conclusions of renewal procedure R/65 and variation II/63)

Action: For adoption of advice to CHMP

7.5.3. Meningococcal group B vaccine (rDNA, component, adsorbed) - BEXSERO (CAP) - EMEA/H/C/002333/MEA 017.2

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: Second interim report for study V72_36OB: an observational safety study after meningococcal B vaccine 4CMenB (Bexsero) vaccination in routine UK care

Action: For adoption of advice to CHMP

7.5.4. Mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - VELPHORO (CAP) - EMEA/H/C/002705/MEA 002.3

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Julie Williams

Scope: Interim results of the VERIFIE study (VFMCRP-MEAF-PA21-01-EU): a non-interventional study to investigate the short and long-term real-life safety, effectiveness, and adherence of Velphoro in patients with hyperphosphataemia undergoing haemodialysis or peritoneal dialysis (PD)

Action: For adoption of advice to CHMP

7.5.5. Strontium ranelate - OSSEOR (CAP) - EMEA/H/C/561/ANX 039.1

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second annual report for an imposed non-interventional safety study to evaluate the effectiveness of the applied risk minimisation measures, including a description of the treated patient population in everyday clinical practice

Action: For adoption of advice to CHMP

7.5.6. Strontium ranelate - PROTELOS (CAP) - EMEA/H/C/560/ANX 039.1

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second annual report for an imposed non-interventional safety study to evaluate the effectiveness of the applied risk minimisation measures, including a description of the treated patient population in everyday clinical practice

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Palonosetron - PALONOSETRON ACCORD (CAP) - EMEA/H/C/004129/LEG 002

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Almath Spooner

Scope: Submission of a six-monthly cumulative review of cases of injection site reactions classified as an important potential risk (1 April-30 September 2016) as requested at the time of the opinion for marketing authorisation(s) for Palonosetron Accord 250 micrograms solution for injection until further market experience is acquired

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. Alipogene tiparvovec - GLYBERA (CAP) - EMEA/H/C/002145/S/0057 (without RMP)

Applicant: uniQure biopharma B.V., ATMP[18]

PRAC Rapporteur: Julie Williams

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.1.2. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0023 (without RMP)

Applicant: Aegerion Pharmaceuticals Limited

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/S/0041 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0006 (with RMP)

Applicant: Baxalta Innovations GmbH

[18] Advanced therapy medicinal product

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/R/0003 (without RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: 1-year conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 MEDIMMUNE (CAP) - EMEA/H/C/003963/R/0003 (without RMP)

Applicant: MedImmune LLC

PRAC Rapporteur: Jan Neuhauser

Scope: 1-year conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Aclidinium bromide - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/R/0031 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Aclidinium bromide - EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/R/0031 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Aliskiren - RASILEZ (CAP) - EMEA/H/C/000780/R/0112 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Ceftaroline fosamil - ZINFORO (CAP) - EMEA/H/C/002252/R/0031 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Follitropin alfa, lutropin alfa - PERGOVERIS (CAP) - EMEA/H/C/000714/R/0050 (without RMP)

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Human normal immunoglobulin - FLEBOGAMMA DIF (CAP) - EMEA/H/C/000781/R/0048 (with RMP)

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Hydroxycarbamide - SIKLOS (CAP) - EMEA/H/C/000689/R/0030 (with RMP)

Applicant: Addmedica

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/R/0052 (with RMP)

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/R/0042 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/R/0037 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Orlistat - ALLI (CAP) - EMEA/H/C/000854/R/0054 (with RMP)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/R/0032 (with RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Zoledronic acid - ZOLEDRONIC ACID MEDAC (CAP) - EMEA/H/C/002359/R/0018 (without RMP)

Applicant: Medac Gesellschaft fur klinische Spezialpraparate GmbH

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

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Parecoxib – DYNASTAT (CAP) - EMEA/H/C/000381/II/0068/G

Applicant: Pfizer Limited

PRAC Rapporteur: Almath Spooner

Scope: PRAC consultation on a grouped variation to: 1) update of section 4.4 of the SmPC in order to update the safety information related to cardiovascular risk information, 2) update of section 4.4 of the SmPC in order to update the safety information related to alcohol use and gastrointestinal (GI) risk, 3) update of section 4.6 of the SmPC in order to update the safety information related to oligohydramnios if the product is used during second or third trimester of pregnancy. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to bring the Product Information in line with the latest QRD template (version 10.0)

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Finasteride (NAP) - SE/H/xxx/WS/139

Applicant: Merck Sharp & Dohme Limited (Propecia, Proscar)

PRAC Lead: Ulla Wändel Liminga

Scope: PRAC consultation on a variation procedure for Propecia, Proscar (finasteride) (SE/H/xxx/WS/139) exploring the possible causal relationship between finasteride 1 mg for the treatment of alopecia and the risk of depression

Action: For adoption of advice to Member States

11.1.2. Racecadotril (NAP) - SE/H/1342/01-03/II/44

Applicant: Bioprojet Europe Ltd (Hidrasec)

PRAC Lead: Qun-Ying Yue

Scope: PRAC consultation on a variation procedure for Hidrasec (racecadotril) (SE/H/1342/01-03/II/44) with regard to interaction with angiotensin converting enzyme (ACE) inhibitors and angioedema occurrence

Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Bendamustine (NAP) - DE/H/1250/001/R/001

Applicant: Astellas Pharma GmbH (Levact)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a renewal procedure for Levact (bendamustine) with regard to safety profile of Levact (bendamustine), strengthening warnings and precautionary measures regarding infections, cardiac disorders, and submission of a direct healthcare professionals communication (DHPC) addressing mainly the issue of increased mortality if bendamustine used off-label and the strengthened warnings on opportunistic infections

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC working group - best practice guide – update on the implementation goals

PRAC lead: Martin Huber, Rafe Suvarna, 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 – report from extraordinary meeting held on 2 December 2016

Action: For discussion

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

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

Action: For discussion

12.3.2. Post-authorisation efficacy studies (PAES) – review of experience

Action: For discussion

12.3.3. PRIority MEdicines (PRIME) - update

Action: For discussion

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. 2017 PRAC work plan

Action: For adoption

12.8. Planning and reporting

12.8.1. PRAC workload statistics

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Sabine Straus

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring – impact on pharmacovigilance performance

Action: For discussion

12.12.3. 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

None

12.13.2. EudraVigilance – annual report 2016

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. EMA Committees – findings of survey to members 2016

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/