14 March 2016
EMA/PRAC/199507/2016 Corr.*
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 14-17 March 2016

Chair: June Raine – Vice-Chair: Almath Spooner

14 March 2016, 13:00 – 19:00, room 3/A

15 March 2016, 08:30 – 19:00, room 3/A

16 March 2016, 08:30 – 19:00, room 3/A

17 March 2016, 08:30 – 16:00, room 3/E

Organisational, regulatory and methodological matters (ORGAM)

31 March 2016, 10:00 - 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).

* Human normal immunoglobulin page 16; HyQvia; Kiovig; Privigen allocated to correct MAHs

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Table of contents

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 14-17 March 2016. See March 2016 PRAC minutes (to be published post April 2016 PRAC meeting).

1.2. Agenda of the meeting of 14-17 March 2016

Action: For adoption

1.3. Minutes of the previous meeting of 08-11 February 2016

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. Direct-acting antivirals (DAAV) indicated for the treatment of hepatitis C (interferon free): daclatasvir – DAKLINZA (CAP); dasabuvir – EXVIERA (CAP); ombitasvir, paritaprevir, ritonavir – VIEKIRAX (CAP); simeprevir - OLYSIO (CAP); sofosbuvir – SOVALDI (CAP); sofosbuvir, ledipasvir – HARVONI (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG (Daklinza); AbbVie Ltd (Exviera, Viekirax); Janssen-Cilag International N.V. (Olysio); Gilead Sciences International Ltd (Harvoni, Sovaldi)

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

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

3.1.2. Gadolinium-containing contrast agents (GdCA): gadobenic acid (NAP); gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP); gadoversetamide – OPTIMARK (CAP)

Applicant: Mallinckrodt Deutschland GmbH (Optimark); various

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

Scope: 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 adoption of a list of questions

3.1.3. Idelalisib – ZYDELIG (CAP)

Applicant: Gilead Sciences International Ltd

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

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

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

3.3.1. Inhaled corticosteroids (ICS)-containing medicinal products indicated in the treatment of chronic obstructive pulmonary disease: beclomethasone (NAP); beclomethasone, formoterol (NAP); budesonide (NAP);

budesonide, formoterol – BIRESP SPIROMAX (CAP); BUDESONIDE FORMOTEROL TEVA (CAP); DUORESP SPIROMAX (CAP); VYALER SPIROMAX (CAP); flunisolide, salbutamol (NAP); fluticasone (NAP); fluticasone, salmeterol (NAP); fluticasone, vilanterol – RELVAR ELLIPTA (CAP); REVINTY ELLIPTA (CAP) – EMEA/H/A-31/1415

Applicant: Glaxo Group Ltd, Teva Pharma B.V., Teva Pharmaceuticals Europe, various

PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Jan Neuhauser

Scope: 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 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[1]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Ferrous sulfate (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of mouth ulceration
Action: For adoption of PRAC recommendation
EPITT 18623 – New signal
Lead Member State: PT

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

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of risk of hyponatremia
Action: For adoption of PRAC recommendation
EPITT 18631 – New signal
Lead Member States: DK, UK, SE

4.1.3. Propofol (NAP)

Applicant: various

[1] 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 diabetes insipidus
Action: For adoption of PRAC recommendation
EPITT 18622 – New signal
Lead Member State: NO

4.2. New signals detected from other sources

4.2.1. Proton pump inhibitors (PPIs): esomeprazole (NAP); lansoprazole (NAP); omeprazole (NAP); pantoprazole – CONTROLOC CONTROL (CAP), PANTECTA CONTROL (CAP), PANTOLOC CONTROL (CAP), PANTOZOL CONTROL (CAP), SOMAC CONTROL (CAP), NAP; rabeprazole (NAP)

Applicant: Takeda GmbH (Controloc Control, Pantecta Control, Pantoloc Control, Pantozol Control, Somac Control), various

PRAC Rapporteur: To be appointed

Scope: Signal of elevated circulating levels of chromogranin A
Action: For adoption of PRAC recommendation
EPITT 18614 – New signal
Lead Member States: UK, AT, FI, NL, SE

4.2.2. Tramadol, paracetamol (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of hyponatraemia and syndrome of inappropriate antidiuretic hormone secretion (SIADH)
Action: For adoption of PRAC recommendation
EPITT 18471 – New signal
Lead Member States: UK, FR

4.3. Signals follow-up and prioritisation

4.3.1. Axitinib – INLYTA (CAP) - EMEA/H/C/002406/SDA/013

Applicant: Pfizer Limited

PRAC Rapporteur: Ingebjorg Buajordet

Scope: Signal of nephrotic syndrome
Action: For adoption of PRAC recommendation
EPITT 18484 – Follow-up to November 2015

4.3.2. Azathioprine (NAP); mercaptopurine - XALUPRINE (CAP), NAP

Applicant: Nova Laboratories Limited (Xaluprine), Aspen Pharma, various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of lymphoproliferative disorders
Action: For adoption of PRAC recommendation
EPITT 18503 – Follow-up to November 2015

4.3.3. Human normal immunoglobulin – FLEBOGAMMA DIF (CAP) - EMEA/H/C/000781/SDA/023; HIZENTRA (CAP) - EMEA/H/C/002127/SDA/019; HYQVIA (CAP) - EMEA/H/C/002491/SDA/005; KIOVIG (CAP) - EMEA/H/C/000628/SDA/039; PRIVIGEN (CAP) - EMEA/H/C/000831/SDA/027, NAP

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

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of posterior reversible encephalopathy syndrome (PRES)
Action: For adoption of PRAC recommendation
EPITT 18512 – Follow-up to November 2015

4.3.4. Loratadine (NAP)

Applicant: various

PRAC Rapporteur: Veerle Verlinden

Scope: Signal of QT prolongation and Torsade de Pointe
Action: For adoption of PRAC recommendation
EPITT 18576 – Follow-up to January 2016

4.3.5. Recombinant factor VIII: antihemophilic factor (recombinant) (NAP) moroctocog alfa – REFACTO AF (CAP) octocog alfa – ADVATE (CAP), HELIXATE NEXGEN (CAP), KOGENATE (CAP)

Applicant: Baxter AG (Advate, Recombinate), Bayer Pharma AG (Kogenate, Helixate NexGen), Pfizer Limited (ReFacto AF), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of inhibitor development in previously untreated patients (PUP)
Action: For adoption of PRAC recommendation
EPITT 18134 – Follow-up to January 2016

4.3.6. Tigecycline – TYGACIL (CAP) - EMEA/H/C/000644/SDA/067

Applicant: Pfizer Limited

PRAC Rapporteur: Miguel-Angel Macia

Scope: Signal of hypofibrinogenaemia
Action: For adoption of PRAC recommendation
EPITT 18479 – Follow-up to November 2015

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Allogeneic T cells genetically modified to express suicide gene - EMEA/H/C/002801, Orphan

Applicant: MolMed SpA, ATMP[2]

Scope: Treatment in haploidentical haematopoietic stem cell transplantation
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.2. Autologous $CD34^+$ enriched cell fraction that contains $CD34^+$ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) cDNA sequence - EMEA/H/C/003854, Orphan

Applicant: GlaxoSmithKline Trading Services, ATMP

Scope: Treatment of severe combined immunodeficiency
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.3. Atazanavir - EMEA/H/C/004048

Scope: Treatment of human immunodeficiency virus (HIV)-1
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.4. Bezlotoxumab - EMEA/H/C/004136

Scope (accelerated assessment): Prevention of *Clostridium difficile* infection (CDI) recurrence
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.5. Bortezomib - EMEA/H/C/004076

Scope: Treatment of multiple myeloma
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.6. Drisapersen - EMEA/H/C/003846, Orphan

Applicant: BioMarin International Limited

Scope: Treatment of Duchenne muscular dystrophy (DMD)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.7. Emtricitabine, rilpivirine, tenofovir alafenamide - EMEA/H/C/004156

Scope: Treatment of human immunodeficiency virus (HIV)-1
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.8. Fluticasone propionate, salmeterol xinafoate - EMEA/H/C/002752; EMEA/H/C/004267

Scope: Treatment of asthma and chronic obstructive pulmonary disease (COPD)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

[2] Advanced-therapy medicinal product

5.1.9. Glycopyrronium bromide - EMEA/H/C/003883

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

5.1.10. Mercaptamine - EMEA/H/C/004038, Orphan

Applicant: Lucane Pharma

Scope: Treatment of corneal cystine deposits
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.11. Miglustat - EMEA/H/C/004016

Scope: Treatment of Gaucher disease
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.12. Pandemic influenza vaccine H5N1 (live attenuated, nasal) - EMEA/H/C/003963

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

5.1.13. Pemetrexed - EMEA/H/C/003895

Scope: Treatment of malignant pleural mesothelioma and non-small cell lung cancer (NSCLC)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.14. Sacubitril, valsartan - EMEA/H/C/004343

Scope: Treatment of heart failure (New York Heart Association (NYHA) class II-IV)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.15. Sofosbuvir, velpatasvir - EMEA/H/C/004210

Scope (accelerated assessment): Treatment of chronic hepatitis C virus
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. Catridecacog – NOVOTHIRTEEN (CAP) - EMEA/H/C/002284/II/0012/G

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Isabelle Robine

Scope: Update of the RMP to include exposure and safety data following finalisation of trial F13CD-3835 (to evaluate the long term safety of monthly replacement therapy with recombinant Factor XIII (rFXIII) when used for prevention of bleeding episodes in paediatric subjects with congenital FXIII A-subunit deficiency). F13CD-3835 was listed as additional pharmacovigilance activity. Update of the RMP to include the final study report of the PRO-RBDD registry (prospective data collection on congenital FXIII deficiency) in the RMP. PRO-RBDD was listed as additional pharmacovigilance activity. The MAH took the opportunity to correct the classification of the additional pharmacovigilance activity PASS NN1841-3868 from category 2 to category 3, as this study is not a specific obligation and is not listed in the Annex II of the Marketing Authorisation
Action: For adoption of PRAC AR

5.2.2. Colistimethate sodium – COLOBREATHE (CAP) - EMEA/H/C/001225/II/0021

Applicant: Forest Laboratories UK Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Update of the RMP (version.6.0) in order to add information on the first interim report for study CLB-MD-05 (an open-label observational safety study of Colobreathe compared with other inhaled antipseudomonal antibiotics in cystic fibrosis patients using cystic fibrosis registries, MEA 009) and the protocol for study CLB-MD-08 (a post-authorisation registry based safety study to evaluate the effectiveness of the risk minimisation educational materials, including DVD and patient and healthcare professional guide, implemented in the EU for Colobreathe)
Action: For adoption of PRAC AR

5.2.3. Pioglitazone – ACTOS (CAP) - EMEA/H/C/000285/WS/0875; GLUSTIN (CAP) - EMEA/H/C/000286/WS/0875 pioglitazone, glimepiride – TANDEMACT (CAP) - EMEA/H/C/000680/WS/0875 pioglitazone, metformin – COMPETACT (CAP) - EMEA/H/C/000655/WS/0875; GLUBRAVA (CAP) - EMEA/H/C/000893/WS/0875

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: Update of the RMP in order to extend the due date for the category 3 drug utilisation study Pioglitazone_5019: from '31 December 2015' to '29 July 2016'
Action: For adoption of PRAC AR

5.2.4. Piperaquine tetraphosphate, artenimol – EURARTESIM (CAP) - EMEA/H/C/001199/II/0020

Applicant: Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP with regards the delay in starting resistance monitoring, collection of off label use data, submission of reports of imposed addition pharmacovigilance activities. The MAH also took this opportunity to reformat the RMP to the new template
Action: For adoption of PRAC AR

5.2.5. Roflumilast – DALIRESP (CAP) - EMEA/H/C/002398/WS/0924; DAXAS (CAP) - EMEA/H/C/001179/WS/0924; LIBERTEK (CAP) - EMEA/H/C/002399/WS/0924

Applicant: Takeda GmbH

PRAC Rapporteur: Miguel-Angel Macia

Scope: To change the final due date to 'Q2 2016' for study RO-2455-302-RD
Action: For adoption of PRAC AR

5.2.6. Teriparatide – FORSTEO (CAP) - EMEA/H/C/000425/II/0042/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 4) and revised protocol for post authorisation safety studies (PASS) B3D-MC-GHBX[2.2] and B3D-MC-GHBX[2.3]. In addition, the RMP has been

updated to include non-uraemic calciphylaxis as a potential important risk as requested by PRAC
Action: For adoption of PRAC AR

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

5.3.1. Abatacept – ORENCIA (CAP) - EMEA/H/C/000701/II/0094/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information with data from the long-term final clinical study report for study IM101174. In addition, the Product Information is being aligned to the latest QRD template (version 9.1). The timelines for study IM101537, aimed at evaluating the effectiveness of risk minimisation measure (alert card) have been updated
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.2. Aflibercept – EYLEA (CAP) - EMEA/H/C/002392/II/0027/G

Applicant: Bayer Pharma AG

PRAC Rapporteur: Isabelle Robine

Scope: Grouped variations to include: 1) 3-year data of the pivotal trials VIVID-DME and VISTA-DME; 2) protocol T data with a consequential update to section 5.1 of the SmPC. Furthermore, the MAH took the opportunity to condense the SmPC section 4.8 text relating to antiplatelet trialists' collaboration (APTC) as recommended by EMA during II/018 variation (diabetic macular oedema (DME) 2 year data), to shorten SmPC section 5.1 as committed by the MAH during II/021 variation (indication myopic choroidal neovascularisation (mCNV)), to align the annexes with the latest QRD templates (version 9.1, June 2015) and to implement minor changes within age-related macular degeneration (AMD) and DME posology sections
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.3. Amifampridine – FIRDAPSE (CAP) - EMEA/H/C/001032/II/0038

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4, 4.5, 5.2 and 5.3 of the SmPC to update the safety information with new data available following the completion of the clinical study report (CSR) REN-002 on renal impairment
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.4. Ataluren – TRANSLARNA (CAP) - EMEA/H/C/002720/II/0019

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Submission of the final results from the non-clinical study PTC124-15055: assessment of uncoupling protein 1 (UCP1) protein levels in brown adipose tissue (BAT) in weanling rats administered ataluren via oral gavage for two weeks, in order to address MEA 007. Part II: module SII of RMP (version 4.4) was updated to reflect in tumor findings that in-vivo exposure to ataluren and the M4 metabolite does not activate BAT. Other sections of the RMP were updated to reflect completion of the study
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.5. Ataluren – TRANSLARNA (CAP) - EMEA/H/C/002720/II/0020

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.4, 4.6, 4.7, 4.8, and 5.1 of the SmPC and Annex II in order to reflect the results from study TC124-GD-020-DMD (SOB 001). The Package Leaflet and the RMP are updated accordingly. In addition, the MAH took the opportunity to include some minor editorial changes throughout the Product Information
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.6. Belimumab – BENLYSTA (CAP) - EMEA/H/C/002015/II/0037

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 5.1 of the SmPC in order to update pharmacodynamic information as the result of completion of efficacy/safety phase 3 continuation study BEL112233 (HGS1006-C1066) which fulfils MEA 011. The RMP has been updated to reflect the completed milestone for this study and to update the information on long-term effects of belimumab on B cells which represents 'missing information' in the current approved RMP
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.7. Bevacizumab – AVASTIN (CAP) - EMEA/H/C/000582/II/0086

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication for the use of Avastin in combination with erlotinib for the first line treatment of patients with unresectable advanced, metastatic or recurrent non-squamous non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) activating mutations. As a consequence sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.8. Brentuximab vedotin – ADCETRIS (CAP) - EMEA/H/C/002455/II/0025

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of adult patients at increased risk of relapse or progression following autologous stem cell transplant (ASCT). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.9. Canakinumab – ILARIS (CAP) - EMEA/H/C/001109/II/0043

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to amend the systemic juvenile idiopathic arthritis (SJIA) indication to include treatment of active Still's disease including adult-onset Still's disease (AOSD) in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the annexes in line with the latest QRD template. An updated RMP (version 10) was provided as part of the application
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.10. Darunavir – PREZISTA (CAP) - EMEA/H/C/000707/II/0078

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study report of the clinical study GS-US-236-0118: phase 3 open-label safety study of cobicistat-containing highly active antiretroviral regimens in human immunodeficiency virus (HIV-1) infected patients with mild to moderate renal impairment (category 3 study in the RMP) in order to update the relevant information on the RMP
Action: For adoption of PRAC Assessment Report

5.3.11. Darunavir, cobicistat – REZOLSTA (CAP) - EMEA/H/C/002819/II/0007

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final study report of the clinical study GS-US-236-0118: phase 3 open-label safety study of cobicistat-containing highly active antiretroviral regimens in human immunodeficiency virus (HIV-1) infected patients with mild to moderate renal impairment (category 3 study in the RMP) in order to update the relevant information in the RMP
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.12. Efavirenz, emtricitabine, tenofovir disoproxil – ATRIPLA (CAP) - EMEA/H/C/000797/WS/0829 emtricitabine, rilpivirine, tenofovir disoproxil – EVIPLERA (CAP) - EMEA/H/C/002312/WS/0829 emtricitabine, tenofovir disoproxil – TRUVADA (CAP) - EMEA/H/C/000594/WS/0829

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd., Gilead Sciences International Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Update of section 4.5 of the SmPCs for Viread, Truvada, Atripla and Eviplera regarding the potential drug interaction with ledipasvir/sofosbuvir (LDV/SOF), as well as that of LDV and SOF as single agents with tenofovir disoproxil fumarate (TDF). The RMP is updated accordingly. In addition, the MAH took the opportunity to update the Product Information according to the latest QRD template (version 9.1) and implement minor linguistic corrections
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.13. Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil – STRIBILD (CAP) - EMEA/H/C/002574/II/0054

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of section 4.5 of the SmPC in order to update the safety information regarding the potential drug interaction with ledipasvir/sofosbuvir (LDV/SOF), as well as that of LDV and SOF as single agents with tenofovir disoproxil fumarate (TDF). The Package

Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to bring the Product Information in line with the latest QRD template (version 9.1)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.14. Entecavir – BARACLUDE (CAP) - EMEA/H/C/000623/II/0049

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of sections 4.8 and 5.1 of the SmPC to add long term efficacy, safety and resistance data on the paediatric population from study AI463189 'expanded cohort' (180 subjects). In adition, the MAH took the opportunity to combine the SmPCs of Baraclude 0.5 mg tablets and Baraclude 1 mg tablets
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.15. Eribulin – HALAVEN (CAP) - EMEA/H/C/002084/II/0028

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication for Halaven 0.44 mg/ml solution for injection for the treatment of soft tissue sarcoma, following the outcome of phase 3 study 309. As a consequence, sections 4.1, 4.4, 4.8, and 5.1 of the SmPC are updated in order to update the safety information. The Package Leaflet and RMP are updated accordingly. In addition, the MAH took the opportunity to update the product information in line with the latest QRD template (version 9.1)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.16. Fentanyl, fentanyl citrate – INSTANYL (CAP) - EMEA/H/C/000959/X/0030/G

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Isabelle Robine

Scope: Line extension to add a new strength of 400 micrograms/dose in a multi-dose nasal spray in pack size of 10's, 20's, 30's and 40 doses; to replace the current multi-dose nasal spray by a new improved child resistant multi-dose nasal spray; to add a new packsize of 30 doses for each current strength (50 micrograms/dose, 100 micrograms/dose and 200 micrograms/dose)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.17. Golimumab – SIMPONI (CAP) - EMEA/H/C/000992/II/0063

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to reflect the data from a multicentre, placebo-controlled, double-blind, randomised-withdrawal, parallel group study (GO KIDS) in children (2 to 17 years of age) with active polyarticular juvenile idiopathic arthritis (pJIA). The Package leaflet is updated accordingly. This procedure includes also an update to the RMP
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.18. 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: Update of section 4.8 of the SmPC in order to update the frequencies of undesirable effects to reflect the final clinical study report from study CSLCT-BIO-08-53 in haemophilia A paediatric patients. The Package Leaflet is updated accordingly. The submission of the final clinical study report for study CSLCT-BIO-08-53 also leads to changes to the RMP (version 6.1) in order to update the Company Core Safety Information (CCSI). Submission of a revised RMP in order to remove 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

5.3.19. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) – CERVARIX (CAP) - EMEA/H/C/000721/II/0067

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include the prevention against premalignant anal lesions and anal cancer as of 9 years of age for Cervarix. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the RMP (version 11.0) including the new indication
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.20. Ibrutinib – IMBRUVICA (CAP) - EMEA/H/C/003791/II/0016

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to broaden the existing indication for chronic lymphocytic leukaemia (CLL) to include all previously untreated patients including those with 17p deletion or TP53 mutation based on the results from the final clinical stuyd report of study PCYC-1115-CA (MEA 021). As a consequence, sections 4.1, 4.6, 4.8, 5.1 and 5.3 of the SmPC are being updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes to the SmPC and to bring Annex II in line with the latest QRD template (version 9.1). Moreover, the updated RMP (version 5.0) has been submitted
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.21. Liraglutide – VICTOZA (CAP) - EMEA/H/C/001026/II/0038

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include second-line monotherapy in type 2 diabetes for Victoza. Additionally, the MAH updated information related to hepatic and renal impairment. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated with new efficacy and safety information. The Package Leaflet is updated in accordance. Furthermore, the MAH took the opportunity to align the PI with the latest QRD template (version 9.1)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.22. Lixisenatide – LYXUMIA (CAP) - EMEA/H/C/002445/II/0013

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to update information on patient with congestive heart failure following submission of the final clinical study report for study EFC11319 (ELIXA) in fulfilment of MEA 001
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.23. Lumacaftor, ivacaftor – ORKAMBI (CAP) - EMEA/H/C/003954/II/0005/G

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

Scope: Submission of the final study reports for the following studies in order to address MEA 006: 1. Report L240: In vitro evaluation of the substrate and inhibitor potential of lumacaftor (VX-809) for breast cancer resistance protein and multidrug resistance protein 2. 2. Report L242: evaluation of the inhibition potential of VX-809 for uptakes transporters OAT1, OAT3, OCT1 and OCT2. 3. L239: In vitro drug-drug interaction studies of the sponsor's test article, VX-770. 4. L241: evaluation of the inhibition potential of VX-770 for uptake transporters OAT1, OAT3, OCT1 and OCT2. An updated RMP (version 2.1) is provided with this variation and includes all the new results of these non-clinical studies. The RMP Public Summary has also been updated to align with the published RMP summary European Public Assessment Report
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.24. Meningococcal group a, c, w135 and y conjugate vaccine – MENVEO (CAP) - EMEA/H/C/001095/II/0056

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.8 of the SmPC in order to add facial paresis as a new adverse drug reaction and to provide further safety information based on the final clinical study report for study V59_34OB in order to fulfil MEA 023. The Package Leaflet is updated accordingly. Moreover, the updated RMP version 8.2 has been submitted
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.25. Natalizumab – TYSABRI (CAP) - EMEA/H/C/000603/II/0077

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adults with highly active relapsing remitting multiple sclerosis with high disease activity despite treatment with at least one modifying therapy (DMT). As a consequence, sections 4.1 and 4.4 of the SmPC are updated in order to provide physicians with more options for treating relapsing remitting multiple sclerosis (RRMS) patients with high disease activity who fail an initial disease modifying therapy (DMT). Consequential changes to sections 4.2, 4.3, 5.1 and Package Leaflet are submitted accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.26. Nepafenac – NEVANAC (CAP) - EMEA/H/C/000818/II/0032

Applicant: Alcon Laboratories (UK) Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication to include the indication 'reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients' also for the 3 mg/ml strength based on data from the phase III studies C-12-067 and C-12-071. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in SmPC and to update the annexes in line with the latest QRD template. An updated RMP (version 7) was provided as part of the application
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.27. Paliperidone – PALIPERIDONE JANSSEN (CAP) - EMEA/H/C/004066/X/0007/G

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variation consisting of an extension application to introduce four new strengths of a once-every-3-month paliperidone injection formulation (175 mg, 263 mg, 350 mg and 525 mg). In addition, extension of indication to revise the injection frequency to ' once-every-3-months' following prior adequate treatment with paliperidone for at least four months. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 are updated. The Package Leaflet and RMP are updated accordingly. In addition, section 1 of SmPC is updated to change the name of the medicinal product from 'Paliperidone Janssen' to 'Trevicta'. Finally, deletion of authorised dosage strengths (i.e. Paliperidone Janssen 25 mg, 50 mg, 75 mg, 100 mg, 150 mg and 150 mg / 100 mg - EU/1/14/971/001-006)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.28. Pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/003820/II/0002

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC with safety and pharmacokinetic (PK) data based on the clinical study report (CSR) of study P006v01. Further, the adverse drug reaction (ADR) Guillain-Barré Syndrome (GBS) has been added to sections 4.4 and 4.8 of the SmPC. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to revise the text referring to fatal cases of pneumonitis in section 4.4 of the SmPC, to implement minor editorial changes in the annexes, to align the SmPC, Annex II, labelling and Package Leaflet with the latest QRD template (version 9.1), and to update the contact details of the local representative in Luxemburg in the Package Leaflet. A revised RMP (version 2.0) was provided as part of the application
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.29. Ponatinib – ICLUSIG (CAP) - EMEA/H/C/002695/II/0029/G

Applicant: Ariad Pharma Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of section 5.3 of the SmPC in order to add pre-clinical information on fertility and early embryonic development to implantation (study 2424-001) and on carcinogenity (study 805826). In addition, the MAH has submitted final study results for pre-clinical studies ARP590, ARP591, ARP592, ARP593, ARP593 on vascular occlusion mechanism and study ARP598 on effects of ponatinib and its metabolites on in vitro kinase activity and

cellular viability following commitments taken during the Article 20 referral procedure (EMEA/H/C/002695/A-20/0003, EC decision on 15 January 2015). No impact in the Product information is proposed for these 6 studies. The RMP has been updated accordingly to the grouped variations
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.30. Posaconazole – NOXAFIL (CAP) - EMEA/H/C/000610/II/0044

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Update of section 4.2 of the SmPC in order to strengthen the information about non-interchangeability of the oral formulations based on new reports of medication errors related to confusion between posaconazole tablets and oral suspension in prescribing. The Package Leaflet and the RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.31. Radium-223 – XOFIGO (CAP) - EMEA/H/C/002653/II/0014/G

Applicant: Bayer Pharma AG

PRAC Rapporteur: Rafe Suvarna

Scope: 1) Submission of clinical study report for study BC1-06, 'a double-blind, randomized, multiple dose, Phase III, multicentre study of alpharadin in the treatment of patients with symptomatic hormone refractory prostate cancer with skeletal metastases' (MEA 001) 2) Submission of clinical study report for study 15995 'Radium-223 dichloride in castration-resistant (hormone-refractory) prostate cancer patients with bone metastases', an early access clinical trial in the USA. (MEA 002) 3) Submission of a clinical study report (based on primary completion) for study 16216 'Radium-223 dichloride in castration-resistant (hormone-refractory) prostate cancer patients with bone metastases' an early access clinical trial outside USA. (MEA 003) 4) The RMP (version 2.0) is updated with regard to the clinical study reports submitted, the due dates in part III section 4, and additionally to reflect the change in SmPC based on the recent reassessment of the primary reference standard for radium-223 (issued by the National Institute of Standards and Technology (NIST)), the active moiety of Xofigo (recently approved EMEA/H/C/2653/II/011)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.32. Rituximab – MABTHERA (CAP) - EMEA/H/C/000165/X/0101/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Line extension to add a new strength: 1,600 mg solution for subcutaneous injection, a new indication is also proposed (different from 1,400 mg strength). Update to the product information of the existing strenghts as a consequence of the line extension application. Update of the RMP to include 'new information' relevant to chronic lymphocytic leukaemia (CLL) and update of the educational materials
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.33. Simeprevir – OLYSIO (CAP) - EMEA/H/C/002777/II/0015

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to amend the safety information regarding the use of Olysio in interferon-free regimens, based on the

primary analysis (SVR12) of studies HPC3017 and HPC3018. The Package Leaflet and Labelling are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.34. Teduglutide – REVESTIVE (CAP) - EMEA/H/C/002345/II/0020

Applicant: NPS Pharma Holdings Limited

PRAC Rapporteur: Torbjorn Callreus

Scope: Extension of indication to include the paediatric population. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated in order to update the safety information. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.35. Tocilizumab – ROACTEMRA (CAP) - EMEA/H/C/000955/II/0057

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with methotrexate (MTX) in the SmPC for the subcutaneous formulation. As a consequence, section 4.1 of the SmPC is updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. Moreover, the updated RMP (version 18) has been submitted
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.36. Ulipristal – ESMYA (CAP) - EMEA/H/C/002041/II/0037

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the safety information based on the results of phase III study PGL11-024
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.37. Varenicline – CHAMPIX (CAP) - EMEA/H/C/000699/II/0062

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: The MAH submitted the final study report of study A3051123 and updated sections 4.4 and 5.1 of the SmPC to reflect these study results. The Annex II, the Package Leaflet and the RMP were also updated accordingly. The MAH took the opportunity to remove the black triangle and to introduce minor amendments to the Labelling
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.38. Vorapaxar – ZONTIVITY (CAP) - EMEA/H/C/002814/II/0005

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: Extension of indication to include treatment of patients with peripheral arterial disease (PAD) and as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the

opportunity to update the contact details of local representative in Luxembourg in the Package Leaflet. Furthermore, the Product Information is brought in line with the latest QRD template (version 9.1). Moreover, revised RMP version 2.0 was provided as part of the application
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. Antithrombin alfa – ATRYN (CAP) - PSUSA/00224/201507

Applicant: GTC Biotherapeutics UK Limited

PRAC Rapporteur: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.2. Asenapine – SYCREST (CAP) - PSUSA/00256/201508

Applicant: N.V. Organon

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.3. Bedaquiline – SIRTURO (CAP) - PSUSA/10074/201509

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.4. Brimonidine – MIRVASO (CAP) - PSUSA/10093/201508 (with RMP)

Applicant: Galderma International

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.5. Cobicistat – TYBOST (CAP) - PSUSA/10081/201508

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.6. Cobicistat, elvitegravir, emtricitabine, tenofovir disoproxil – STRIBILD (CAP) - PSUSA/10082/201508

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.7. Collagenase clostridium histolyticum – XIAPEX (CAP) - PSUSA/00871/201508

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.8. Copper (^{64}Cu) chloride – CUPRYMINA (CAP) - PSUSA/10040/201508

Applicant: Sparkle S.r.l.

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.9. Crizotinib – XALKORI (CAP) - PSUSA/10042/201508

Applicant: Pfizer Limited

PRAC Rapporteur: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.10. Dabrafenib – TAFINLAR (CAP) - PSUSA/10084/201508

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.11. Deferiprone – FERRIPROX (CAP) - PSUSA/00940/201508 (with RMP)

Applicant: Apotex Europe BV

PRAC Rapporteur: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.12. Dronedarone – MULTAQ (CAP) - PSUSA/01180/201507

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.13. Elosulfase alfa – VIMIZIM (CAP) - PSUSA/10218/201508

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.14. Elvitegravir – VITEKTA (CAP) - PSUSA/02577/201508

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.15. Emtricitabine, rilpivirine, tenofovir disoproxil – EVIPLERA (CAP) - PSUSA/09142/201508

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.16. Enzalutamide – XTANDI (CAP) - PSUSA/10095/201508 (with RMP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.17. Ex vivo expanded autologous human corneal epithelial cells containing stem cells – HOLOCLAR (CAP) - PSUSA/10352/201508

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CAT/CHMP

6.1.18. Florbetaben (^{18}F) – NEURACEQ (CAP) - PSUSA/10094/201508

Applicant: Piramal Imaging Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Human coagulation factor VIII, von Willebrand factor complex – VONCENTO (CAP) - PSUSA/10102/201508

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.20. Idelalisib – ZYDELIG (CAP) - PSUSA/10303/201509

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.21. Influenza vaccine (split virion, inactivated) – IDFLU (CAP); INTANZA (CAP) - PSUSA/01743/201508

Applicant: Sanofi Pasteur

PRAC Rapporteur: Miguel-Angel Macia

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.22. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) – OPTAFLU (CAP) - PSUSA/01745/201508

Applicant: Novartis Influenza Vaccines Marburg GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.23. Interferon beta-1b – BETAFERON (CAP); EXTAVIA (CAP) - PSUSA/01759/201507

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.24. Lamivudine – ZEFFIX (CAP) - PSUSA/01824/201507

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.25. Lenvatinib – LENVIMA (CAP) - PSUSA/10380/201508

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.26. Linaclotide – CONSTELLA (CAP) - PSUSA/10025/201508

Applicant: Almirall S.A

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.27. Loxapine – ADASUVE (CAP) - PSUSA/10113/201508

Applicant: Ferrer Internacional S.A.

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.28. Maraviroc – CELSENTRI (CAP) - PSUSA/01934/201508

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.29. Mecasermin – INCRELEX (CAP) - PSUSA/01942/201508

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.30. Metformin hydrochloride, sitagliptin – EFFICIB (CAP); JANUMET (CAP); RISTFOR (CAP); VELMETIA (CAP) - PSUSA/02003/201508

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.31. Midazolam – BUCCOLAM (CAP) - PSUSA/10118/201509

Applicant: Shire Services BVBA

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.32. Natalizumab – TYSABRI (CAP) - PSUSA/02127/201508

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.33. Nonacog alfa – BENEFIX (CAP) - PSUSA/02183/201508

Applicant: Pfizer Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.34. Ospemifene – SENSHIO (CAP) - PSUSA/10340/201508

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.35. Pandemic influenza vaccine H5N1 (whole virion, vero cell derived, inactivated), prepandemic influenza vaccine H5N1 (whole virion, vero cell derived, inactivated) – PANDEMIC INFLUENZA VACCINE H5N1 BAXTER (CAP); VEPACEL (CAP) - PSUSA/02282/201508

Applicant: Nanotherapeutics Bohumil Sro

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.36. Pembrolizumab – KEYTRUDA (CAP) - PSUSA/10403/201509

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.37. Pomalidomide – IMNOVID (CAP) - PSUSA/10127/201508 (with RMP)

Applicant: Celgene Europe Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.38. Pyronaridine, artesunate – PYRAMAX (Art 58[3]) – EMA/H/W/002319/PSUV/0012

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.39. Safinamide – XADAGO (CAP) - PSUSA/10356/201508

Applicant: Zambon SpA

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.40. Teduglutide – REVESTIVE (CAP) - PSUSA/09305/201508

Applicant: NPS Pharma Holdings Limited

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.41. Vemurafenib – ZELBORAF (CAP) - PSUSA/09329/201508

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.42. Vernakalant hydrochloride – BRINAVESS (CAP) - PSUSA/03109/201508 (with RMP)

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.43. Zoledronic acid – ACLASTA (CAP) - PSUSA/09334/201508

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

[3] Article 58 of Regulation (EC) No 726/2004 allows the Agency's Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO), on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

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

6.2.1. Eflornithine – VANIQA (CAP), NAP - PSUSA/01202/201507

Applicant: Almirall S.A

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.2.2. Human protein C – CEPROTIN (CAP), NAP - PSUSA/02563/201507

Applicant: Baxter AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.2.3. Pioglitazone - ACTOS (CAP), GLUSTIN (CAP), NAP; pioglitazone, glimepiride – TANDEMACT (CAP); pioglitazone, metformin - COMPETACT (CAP), GLUBRAVA (CAP) - PSUSA/02417/201507

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

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. Albendazole (NAP) - PSUSA/00000073/201507

Applicant: various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.2. Alprostadil (patency of the ductus arteriosus) (NAP) - PSUSA/00010021/201507

Applicant: various

PRAC Lead: Marianne Lunzer

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.3. Chloroquine (NAP) - PSUSA/00000685/201508

Applicant: various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.4. Cisatracurium (NAP) - PSUSA/00000777/201507

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.5. Diphtheria, tetanus, pertussis (acellular, component) and poliomyelitis (inactivated) vaccine (adsorbed); diphtheria, tetanus, pertussis (acellular, component) and poliomyelitis (inactivated) vaccine (adsorbed) reduce antigens content (NAP) - PSUSA/00001126/201507

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.6. Escherichia coli lysate (NAP) - PSUSA/00001263/201507

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.7. Ethinylestradiol, gestodene (transdermal application) (NAP) - PSUSA/00010145/201508

Applicant: various

PRAC Lead: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.8. Everolimus (indicated for rejection of transplanted organs) (NAP) - PSUSA/00010269/201507

Applicant: various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.9. Fluticasone propionate, formoterol fumarate dihydrate (NAP) - PSUSA/00010339/201507

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.10. Fosinopril (NAP) - PSUSA/00001474/201507

Applicant: various

PRAC Lead: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.11. Fosinopril, hydrochlorothiazide (NAP) - PSUSA/00001475/201507

Applicant: various

PRAC Lead: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.12. Gaxilose (NAP) - PSUSA/00010283/201507

Applicant: various

PRAC Lead: Miguel-Angel Macia

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.13. Lisdexamfetamine (NAP) - PSUSA/00010289/201508

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.14. Lubiprostone (NAP) - PSUSA/00010290/201507

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.15. Magnesium sulfate, sodium sulfate, potassium sulfate (NAP) - PSUSA/00010239/201508

Applicant: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.16. Montelukast (NAP) - PSUSA/00002087/201507

Applicant: various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.17. Paracetamol, tramadol (NAP) - PSUSA/00002310/201508

Applicant: various

PRAC Lead: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.18. Poliovirus type 1, poliovirus type 3 (oral, live, attenuated) vaccine (NAP) - PSUSA/00002460/201507

Applicant: various

PRAC Lead: Jean-Michel Dogne

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.19. Ribavirin (aerosol application) (NAP) - PSUSA/00010003/201508

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.20. Thiocolchicoside (NAP) - PSUSA/00002927/201507

Applicant: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.21. Tiapride (NAP) - PSUSA/00002944/201507

Applicant: various

PRAC Lead: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.22. Trimetazidine (NAP) - PSUSA/00003043/201508

Applicant: various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.23. Ziprasidone (NAP) - PSUSA/00003146/201507

Applicant: various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Caspofungin – CANCIDAS (CAP) - EMEA/H/C/000379/LEG/062

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Veerle Verlinden

Scope: Following PSUSA/00000576/201412, the MAH was requested to provide a cumulative analysis of the risk of serious cutaneous adverse reactions (SCARs) (including Stevens–Johnson syndrome, toxic epidermal necrolysis and drug reaction with eosinophilia and systemic symptoms) with the cut-off date 30.09.2015

Action: For adoption of recommendation to CHMP

6.4.2. Human rotavirus, live attenuated – ROTARIX (CAP) - EMEA/H/C/000639/LEG 086

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: The MAH provided updated analyses on hypersensitivity case of clinical data and post-marketing data and provided a case definition for hypersensitivity taking into account the definition of the international consensus on drug allergy for the case review, as requested during the renewal procedure R/0079. The search for cumulative analysis should include MedDRA[4] preferred terms (PTs) for narrow Standardised MedDRA Queries (SMQ) narrow for hypersensitivity excluding PTs indicative of a site-specific reaction (injection site, vaccination site)
Action: For adoption of advice to CHMP

6.4.3. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP) - EMEA/H/C/002617/LEG 007.1

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's responses to LEG 007 on prevention of administration of expired Fluenz Tetra as per request for supplementary information adopted in June 2015: the MAH should suggest measures to increase attention to expiration dates, although spontaneous reports are not a reliable basis for assessing actual incidence rates, by end of Q4 2015 (deadline proposed by MAH)
Action: For adoption of advice to CHMP

[4] Medical Dictionary for Regulatory Activities

6.4.4. Vildagliptin – GALVUS (CAP) - EMEA/H/C/00771/LEG 042 ; JALRA - EMEA/H/C/001048/LEG 026; XILIARX - EMEA/H/C/001051/LEG 026; Vildagliptin, metformin hydrochloride – EUCREAS (CAP) - EMEA/H/C/000807/LEG 024; ICANDRA (CAP) - EMEA/H/C/001050/LEG 022; ZOMARIST (CAP) - EMEA/H/C/001049/LEG 022

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's responses to the request from PRAC following the assessment of PSUSA/00003113/201502 regarding acute renal failure cases with vildagliptin (Galvus/Eucreas)
Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[5]

7.1.1. Afamelanotide – SCENESSE (CAP) - EMEA/H/C/PSP/0022.1.A.1

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Revised PASS protocol for study CUV-PA001: disease registry to assess long-term safety and generate data on the clinical benefits of afamelanotide 16 mg implant in patients with erythropoietic protoporphyria (EPP)
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.2. Deferasirox – EXJADE (CAP) - EMEA/H/C/PSP/0010.4.A.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Revised PASS protocol for study CICL670E2422: observational cohort study in paediatric non transfusion dependant-thalassaemia (NTDT) patients over 10 years
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.3. Ethinylestradiol and ethinylestradiol, levonorgestrel (NAP) - EMEA/H/N/PSP/0037

Applicant: Teva Pharma B.V. (Seasonique)

PRAC Rapporteur: Isabelle Robine

Scope: Draft protocol for a post-authorisation safety study to assess the risk of venous thromboembolic events (VTE) in women exposed to Seasonique: a retrospective longitudinal cohort study assessing the safety of short and long-term use of Seasonique
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.4. Ferric citrate coordination complex – FEXERIC (CAP) - EMEA/H/C/PSP/0038

Applicant: Keryx Biopharma UK Ltd.

PRAC Rapporteur: Julie Williams

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

Scope: Draft protocol for a non-interventional observational post-authorisation study to assess the safety of Fexeric as a phosphate binder in routine clinical practice
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.5. Ketoconazole – KETOCONAZOLE HRA (CAP) - EMEA/H/C/PSP/0040

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: Drat protocol for a post-authorisation safety study: a multi-country, observational registry to collect clinical information on patients with Cushing syndrome patients exposed to ketoconazole (preferably using the existing European Registry on Cushing's syndrome (ERCUSYN) registry), to assess drug utilisation patterns and to document the safety and effectiveness of ketoconazole
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.6. Pitolisant – WAKIX (CAP) - EMEA/H/C/PSP/0039

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Draft protocol for a non-interventional post-authorisation safety study (PASS): a multi-centre, observational post-authorisation safety study to document the drug utilisation of Wakix and to collect information on the safety of Wakix when used in routine medical practice
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.7. Thiocolchicoside (NAP) - EMEA/H/N/PSP/j/0030.1

Applicant: Sanofi-Aventis Recherche & Développement and other companies involved in the consortium

PRAC Rapporteur: Amelia Cupelli

Scope: Revised protocol for a drug utilisation study to characterise prescribing practices for the medicinal products during typical clinical use in representative groups of prescribers and to assess main reasons for prescription
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.8. Tolvaptan – JINARC (CAP) - EMEA/H/C/PSP/0028.2

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Revised PASS protocol for a prospective study of the safety of tolvaptan in autosomal dominant polycystic kidney disease (ADPKD) patients with an additional retrospective component to assess for risks associated with long term use
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[6]

7.2.1. Dasabuvir – EXVIERA (CAP) - EMEA/H/C/003837/MEA/001.2

Applicant: AbbVie Ltd.

PRAC Rapporteur: Miguel-Angel Macia

Scope: MAH's responses to MEA 001.1 [PASS protocol for a prospective, observational cohort study utilising the hepatitis C therapeutic registry and research network (HCV-TARGET) data to evaluate the clinical impact and real world frequency of Grade 3+ ALT elevations in patients being treated for hepatitis C with paritaprevir with ritonavir (paritaprevir/ritonavir), ombitasvir and dasabuvir (3 direct-acting antiviral (DAA) regimen) or paritaprevir/ritonavir and ombitasvir (2-DAA regimen) with or without ribavirin for hepatitis C infection (HCV) (SHORT – evaluation of the potential for and clinical impact of increased ALT in patients using the AbbVie 2-DAA or 3-DAA Regimens in a real world setting)] as per request for supplementary information adopted in October 2015
Action: For adoption of advice to CHMP

7.2.2. Edoxaban – LIXIANA (CAP) - EMEA/H/C/002629/MEA/005.1

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 005 [drug utilisation study DSE-EDO-01-14-EU: edoxaban prescription patterns in Europe: a retrospective drug utilisation chart review study] as per request for supplementary information adopted in October 2015
Action: For adoption of advice to CHMP

7.2.3. Edoxaban – LIXIANA (CAP) - EMEA/H/C/002629/MEA/006.1

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 006 [PASS Protocol Study DSE-EDO-04-14-EU] as per request for supplementary information as adopted in October 2015
Action: For adoption of advice to CHMP

7.2.4. Edoxaban – LIXIANA (CAP) - EMEA/H/C/002629/MEA/007.1

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 007 [PASS protocol study DSE-EDO-05-14-EU] as per request for supplementary information adopted in October 2015
Action: For adoption of advice to CHMP

7.2.5. Evolocumab – REPATHA (CAP) - EMEA/H/C/003766/MEA/009

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

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

Scope: Draft protocol for study 20150162: a multi-national observational study to evaluate the safety of Repatha in pregnancy
Action: For adoption of advice to CHMP

7.2.6. Filgrastim – NIVESTIM (CAP) - EMEA/H/C/001142/MEA 015.1

Applicant: Hospira UK Limited

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's responses to MEA 015 [revised protocol for study ZOB-NIV-1513: a multinational, multicentre, prospective, non-interventional, post-authorisation safety study in healthy donors (HDs) exposed to Nivestim for haematopoietic stem cell (HSC) mobilisation (NEST)] as per request for supplementary information adopted in January 2016
Action: For adoption of advice to CHMP

7.2.7. Infliximab – REMICADE (CAP) - EMEA/H/C/000240/MEA/133.10

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Eighth annual paediatric inflammatory bowel disease (IBD) registry (DEVELOP) report
Action: For adoption of advice to CHMP

7.2.8. Insulin lispro – HUMALOG (CAP) - EMEA/H/C/000088/MEA/028.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 028.1 [US surveillance programme] as per request for supplementary information adopted in October 2015
Action: For adoption of advice to CHMP

7.2.9. Insulin lispro - LIPROLOG (CAP) - EMEA/H/C/000393/MEA/021.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 028.1 [US surveillance programme] as per request for supplementary information adopted in October 2015
Action: For adoption of advice to CHMP

7.2.10. Interferon beta-1a – AVONEX (CAP) - EMEA/H/C/000102/MEA/084.4

Applicant: Biogen Idec

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's responses to MEA 084.3 [PASS protocol: pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon-beta – a register-based study in the Nordic countries] as per request for supplementary information adopted in November 2015
Action: For adoption of advice to CHMP

7.2.11. Interferon beta-1a – REBIF (CAP) - EMEA/H/C/000136/MEA/039.4

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's responses to MEA 039.3 [PASS protocol: pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon-beta – a register-based study in the Nordic countries] as per request for supplementary information adopted in November 2015
Action: For adoption of advice to CHMP

7.2.12. Interferon beta-1b – BETAFERON (CAP) - EMEA/H/C/000081/MEA/021.4

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 021.3 [PASS protocol: pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon-beta – a register-based study in the Nordic countries] as per request for supplementary information adopted in November 2015
Action: For adoption of advice to CHMP

7.2.13. Interferon beta-1b – EXTAVIA (CAP) - EMEA/H/C/000933/MEA/019.4

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 019.3 [PASS protocol: pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon-beta – a register-based study in the Nordic countries] as per request for supplementary information adopted in November 2015
Action: For adoption of advice to CHMP

7.2.14. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/MEA/008.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's responses to MEA 008 [Protocol for study CA209234, a non-interventional category 3 PASS: pattern of use, safety, and effectiveness of nivolumab in routine oncology practice] as per request for supplementary information adopted in November 2015
Action: For adoption of advice to CHMP

7.2.15. Ombitasvir, paritaprevir, ritonavir – VIEKIRAX (CAP) - EMEA/H/C/003839/MEA/001.2

Applicant: AbbVie Ltd.

PRAC Rapporteur: Miguel-Angel Macia

Scope: MAH's responses to MEA 001.1 [observational, cohort study utilising the hepatitis C therapeutic registry & research network (HCV-TARGET)] as per request for supplementary information adopted in October 2015
Action: For adoption of advice to CHMP

7.2.16. Ustekinumab – STELARA (CAP) - EMEA/H/C/000958/MEA/044

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Draft protocol for an adolescent registry: an observational post-authorisation safety study of ustekinumab in the treatment of pediatric patients aged 12 years and older with moderate to severe plaque psoriasis
Action: For adoption of advice to CHMP

7.2.17. Vernakalant – BRINAVESS (CAP) - EMEA/H/C/001215/MEA/026.1

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 026 [Amendment to PASS protocol for vernakalant intravenous (IV) sterile concentrate prospective safety registry study: a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant IV sterile concentrate (study 6621 049-00)] as per request for supplementary information adopted in September 2015
Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[7]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[8]

7.4.1. Abacavir – ZIAGEN (CAP) - EMEA/H/C/000252/WS/0769 lamivudine – EPIVIR (CAP) - EMEA/H/C/000107/WS/0769, LAMIVUDINE VIIV (Art 58[9]) - EMEA/H/W/000673/WS/0769 lamivudine, abacavir – KIVEXA (CAP) - EMEA/H/C/000581/WS/0769 lamivudine, abacavir, zidovudine – TRIZIVIR (CAP) - EMEA/H/C/000338/WS/0769 lamivudine, zidovudine – COMBIVIR (CAP) - EMEA/H/C/000190/WS/0769 (without RMP)

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Isabelle Robine

Scope: Submission of final clinical study report (CSR) for mitochondrial toxicity in children (MITOC) study (WE027/WWE112888). The MAH took also the opportunity to respond to a LEG on mitochondrial dysfunction to address the request on revision of class labelling of antiretrovirals on mitochondrial toxicity
Action: For adoption of PRAC Assessment Report

7.4.2. Dabigatran etexilate – PRADAXA (CAP) - EMEA/H/C/000829/II/0092

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

[7] In accordance with Article 107p-q of Directive 2001/83/EC
[8] 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
[9] Article 58 of Regulation (EC) No 726/2004 allows the Agency's Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO), on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

Scope: Submission of the final study report for observational study 1160. 157 comparing the safety and efficacy of Pradaxa versus warfarin in the real world in patients with non-valvular atrial fibrillation. The RMP (version 31.3) has been updated with results from the observational study 1160.157 and inclusion of information on study 1160.207. In addition, the MAH took the opportunity to consolidate previous RMP versions and add information on study 1160.118 as the results were submitted with procedure II/91
Action: For adoption of PRAC Assessment Report

7.4.3. Eptacog alfa (activated) – NOVOSEVEN (CAP) - EMEA/H/C/000074/II/0089

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Sabine Straus

Scope: Submission of the final study teport for study NN7025-3601 : a prospective observational study on NovoSeven room temperature (VII25) in patients with haemophilia A and B. The submission of this study report addresses MEA 046.4 and an updated RMP (version 6.1) is provided accordingly
Action: For adoption of PRAC Assessment Report

7.4.4. Meningococcal group a, c, w135 and y conjugate vaccine – MENVEO (CAP) - EMEA/H/C/001095/II/0062

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final clinical study report for study V59_54OB, a post-licensure observational safety surveillance study of Menveo vaccination in children 2 through 10 years of age, in order to update the safety information of Menveo in subjects aged 2-10 years of age to fulfil MEA 024
Action: For adoption of PRAC Assessment Report

7.4.5. Saxagliptin – ONGLYZA (CAP) - EMEA/H/C/001039/WS/0897 saxagliptin, metformin hydrochloride – KOMBOGLYZE (CAP) - EMEA/H/C/002059/WS/0897

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a final clinical study report for an epidemiological study CV181-102 with the aim to assess risk factors associated with low lymphocyte count in patients with T2DM (PASS study category 3 currently in the RMP) together with an updated RMP (version 10)
Action: For adoption of PRAC Assessment Report

7.4.6. Tacrolimus – PROTOPIC (CAP) - EMEA/H/C/000374/II/0063

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Almath Spooner

Scope: Submission of the final clinical study report of the non-interventional, registry PASS study JOELLE (JOint European Longitudinal Lymphoma and skin cancer Evaluation) final results. The RMP was updated accordingly
Action: For adoption of PRAC Assessment Report

7.4.7. Voriconazole – VFEND (CAP) - EMEA/H/C/000387/II/0115

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Submission of the final study report for a non-interventional post authorisation safety study A1501097: evaluation of the potential association between voriconazole use and squamous cell carcinoma (SCC) of the skin among patients with lung or lung/heart transplants in order to fulfil MEA 071.11. Consequently, the RMP (version 4.0) was updated
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[10]

7.5.1. Catridecacog – NOVOTHIRTEEN (CAP) - EMEA/H/C/002284/MEA/015

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Isabelle Robine

Scope: First interim study report for study NN1841-3868: use of recombinant factor XIII in treatment of congenital factor XIII deficiency, a prospective multicentre observational study
Action: For adoption of advice to CHMP

7.5.2. Mannitol – BRONCHITOL (CAP) - EMEA/H/C/001252/ANX/002.8

Applicant: Pharmaxis Pharmaceuticals Limited

PRAC Rapporteur: Julie Williams

Scope: Sixth interim analysis of the cystic fibrosis (CF) study
Action: For adoption of advice to CHMP

7.5.3. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) – OPTAFLU (CAP) - EMEA/H/C/000758/MEA/050.2

Applicant: Novartis Influenza Vaccines Marburg GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim results of the enhanced passive safety surveillance of the seasonal cell culture trivalent influenza vaccine (Optaflu) for the 2015-16 influenza season in England in the pharmacies setting (V58_41OB)
Action: For adoption of advice to CHMP

7.5.4. Ivacaftor – KALYDECO (CAP) - EMEA/H/C/002494/ANX/001.3

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Miguel-Angel Macia

Scope: Third interim study results of a five-year long-term observational study with ivacaftor in patients with cystic fibrosis, including also microbiological and clinical endpoints
Action: For adoption of advice to CHMP

[10] In line with the revised variations regulation for any submission before 4 August 2013

7.5.5. Oseltamivir – TAMIFLU (CAP) - EMEA/H/C/000402/LEG/087.3

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Third annual review on pregnancy cases
Action: For adoption of recommendation to CHMP

7.5.6. Oseltamivir – TAMIFLU (CAP) - EMEA/H/C/000402/MEA/102.1

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Annual review of the safety and efficacy of oseltamivir in immunocompromised patients up to final submission of the clinical trial NV20234 study report (treatment) as flu and season permits
Action: For adoption of advice to CHMP

7.5.7. Perampanel – FYCOMPA (CAP) - EMEA/H/C/002434/MEA/004.3

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Julie Williams

Scope: Annual progress report for a post-marketing observational safety study to evaluate the long-term safety and tolerability of Fycompa as add-on therapy in epilepsy patients (PASS study E2007-G000-402)
Action: For adoption of advice to CHMP

7.5.8. Plasmodium falciparum and hepatitis b vaccine (recombinant, adjuvanted) – MOSQUIRIX (Art 58[11]) - EMEA/H/W/002300/MEA/001

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: First annual report for study Malaria-076, an open extension to the study Malaria-055 to evaluate long-term efficacy, safety and immunogenicity of the RTS,S/AS01E candidate vaccine (Mosquirix) against malaria disease caused by Plasmodium falciparum in infants and children in Africa, describing the incidence of severe malaria in the long-term over a 3-year period (from January 2014 to December 2016) of follow-up pooled across transmission settings, in both age categories: infants 6-12 weeks and children aged 5 to 17 months
Action: For adoption of advice to CHMP

7.5.9. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/000944/ANX/033.1

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Interim results from pharmacoepidemiological study of rivaroxaban use and potential adverse outcomes in routine clinical practice in Germany, the Netherlands, the UK and Sweden

[11] Article 58 of Regulation (EC) No 726/2004 allows the Agency's Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO), on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

Action: For adoption of advice to CHMP

7.5.10. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/000944/ANX/035.1

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Second interim report an observational post-authorization Modified Prescription-Event Monitoring safety study (M-PEM) to monitor the safety and utilisation of rivaroxaban for the prevention of stroke in patients with atrial fibrillation (AF), treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE following an acute DVT in the primary care setting in England – including an extension to the rivaroxaban M-PEM study to include acute coronary syndrome patients
Action: For adoption of advice to CHMP

7.5.11. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/000944/MEA/023.2

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Interim results (wave 1) of study SN 16167, a survey regarding educational materials for prescriber and patients receiving rivaroxaban for stroke prevention or deep vein thrombosis treatment post-launch
Action: For adoption of advice to CHMP

7.5.12. Tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/MEA/256.6

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Interim results for a drug utilisation study (DUS) GS-EU-104-0433 in paediatric patients with human immunodeficiency virus (HIV-1) infection, to describe the characteristics of HIV-1 infected patients up to 18 years of age treated with Viread within the EU in order to determine if they are being managed in accordance with the European SmPC
Action: For adoption of advice to CHMP

7.5.13. Tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/MEA/265.5

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Interim results for study GS-EU-174-1403, a pharmacoepidemiology study to define the long-term safety profile of tenofovir disoproxil fumarate and describe the management of associated renal and bone toxicity in Chronic Hepatitis B -infected adolescents aged 12 to <18 years in Europe
Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Eliglustat – CERDELGA (CAP) - EMEA/H/C/003724/ANX/001.1

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's responses to ANX 001 [Safety sub-registry study OBS14099: concept protocol for a prospective multicentre observational post authorisation safety sub-registry to characterize the long-term safety profile of eliglustat of adult patients with Gaucher disease] as per request for supplementary information adopted in september 2015
Action: For adoption of advice to CHMP

7.6.2. Pandemic influenza vaccine (H1N1)v (split virion, inactivated, adjuvanted) – PANDEMRIX (CAP) - EMEA/H/C/000832/MEA 122

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Rafe Suvarna

Scope: Final study report for PASS study EPI-FLU H1N1-014 VS: an observational retrospective database analysis to estimate the risk of multiple sclerosis following vaccination with Arepanrix in Manitoba, Canada
Action: For adoption of advice to CHMP

7.7. New 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.

7.8. Ongoing 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.

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

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

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

8.1. Annual reassessments of the marketing authorisation

None

8.2. Conditional renewals of the marketing authorisation

8.2.1. Fampridine – FAMPYRA (CAP) - EMEA/H/C/002097/R/0029 (without RMP)

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Abiraterone – ZYTIGA (CAP) - EMEA/H/C/002321/R/0038 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.2. Aztreonam – CAYSTON (CAP) - EMEA/H/C/000996/R/0058 (without RMP)

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Sabine Straus

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.3. C1-esterase inhibitor, human – CINRYZE (CAP) - EMEA/H/C/001207/R/0040 (without RMP)

Applicant: Shire Services BVBA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.4. Dexmedetomidine – DEXDOR (CAP) - EMEA/H/C/002268/R/0019 (with RMP)

Applicant: Orion Corporation

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.5. Levetiracetam – LEVETIRACETAM TEVA (CAP) - EMEA/H/C/002316/R/0021 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Veerle Verlinden

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.6. Levodopa, carbidopa, entacapone – LEVODOPA, CARBIDOPA, ENTACAPONE ORION (CAP) - EMEA/H/C/002441/R/0019 (without RMP)

Applicant: Orion Corporation

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.7. Midazolam – BUCCOLAM (CAP) - EMEA/H/C/002267/R/0032 (with RMP)

Applicant: Shire Services BVBA

PRAC Rapporteur: Sabine Straus

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.8. Perflutren – LUMINITY (CAP) - EMEA/H/C/000654/R/0021 (without RMP)

Applicant: Lantheus MI UK Ltd

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.9. Telavancin – VIBATIV (CAP) - EMEA/H/C/001240/R/0025 (without RMP)

Applicant: Clinigen Healthcare Ltd

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.10. Vismodegib – ERIVEDGE (CAP) - EMEA/H/C/002602/R/0023 (without RMP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

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.

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. Efavirenz, emtricitabine, tenofovir disoproxil – ATRIPLA (CAP) - EMEA/H/C/000797/WS/0792 elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil – STRIBILD (CAP) - EMEA/H/C/002574/WS/0792 emtricitabine – EMTRIVA (CAP) - EMEA/H/C/000533/WS/0792 emtricitabine, rilpivirine, tenofovir disoproxil – EVIPLERA (CAP) - EMEA/H/C/002312/WS/0792 emtricitabine, tenofovir disoproxil – TRUVADA (CAP) - EMEA/H/C/000594/WS/0792 tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/WS/0792

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd., Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of section 4.4 of the SmPC in order to delete the human immunodeficiency virus (HIV) class label wording for mitochondrial dysfunction following the review of existing data on mitochondrial toxicity including the Mitochondrial Toxicity in Children (MITOC) study. The Package Leaflets for Viread, Truvada and Emtriva are updated accordingly
Action: For adoption of advice to CHMP

10.1.2. Posaconazole – NOXAFIL (CAP) - EMEA/H/C/000610/II/0044

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Update of section 4.2 of the SmPC in order to strengthen the information about non-interchangeability of the oral formulations based on new reports of medication errors related to confusion between posaconazole tablets and oral suspension in prescribing. The Package Leaflet and the RMP are updated accordingly
Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

12.2.1. Joint Paediatric Committee (PDCO)-PRAC Working Group – summary of the joint PDCO-PRAC strategic review and learning meeting, 28-29 May 2015

PRAC lead: June Raine
Action: For discussion

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

12.3.1. Scientific Advice Working Party (SAWP) – consultation procedure: criteria and process

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. EMA reflection paper on extrapolation across age groups

PRAC lead: Jolanta Gulbinovič
Action: For adoption

12.4.2. Strengthening Collaborations for Operating Pharmacovigilance in Europe (SCOPE)

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections - inspectors/assessors' collaboration and sharing of pharmacovigilance inspection information

Action: For discussion

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst; Margarida Guimarães
Action: For discussion

12.10.3. PSUR action group - roadmap for PSUR issues: draft outcome and next steps

PRAC lead: Almath Spooner; Jolanta Gulbinovic; Margarida Guimaraes; Menno van der Elst
Action: For discussion

12.10.4. PSURs repository

None

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

Action: For adoption of the revised list

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 - collecting and reporting information on off-label use - discussion paper

Action: For adoption

12.12.2. Additional monitoring

None

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

Action: For adoption of the list

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public hearings - draft rules of procedure

Action: For discussion

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. EMA emergency notification system

Action: For discussion

12.20.2. Initial marketing authorisation(s) - revised accelerated assessment procedural timetables – follow up

PRAC lead: Ulla Wändel Liminga
Action: For discussion

12.20.3. Pharmacovigilance programme and revised implementation

Action: For discussion

13. Any other business

None

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/