24 October 2016
EMA/PRAC/637685/2016
Inspections, Human Medicines Pharmacovigilance & Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 24-27 October 2016

Chair: June Raine – Vice-Chair: Almath Spooner

24 October 2016, 13:00 – 19:30, room 3/A

25 October 2016, 08:30 – 19:30, room 3/A

26 October 2016, 08:30 – 19:30, room 3/A

27 October 2016, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

10 November 2016, 09:00 – 12:00, room 7/B, via Adobe Connect

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 24-27 October 2016. See November 2016 PRAC minutes (to be published post December 2016 meeting).

1.2. Adoption of agenda of the meeting of 24-27 October 2016

Action: For adoption

1.3. Adoption of the minutes of the previous meeting of 26-29 September 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

None

3.2. Ongoing procedures

3.2.1. 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) - EMEA/H/A-20/1438

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: Margarida Guimarães; PRAC Co-rapporteur: Dolores Montero Corominas

Scope: Review of the benefit-risk balance of DAAV 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 outstanding issues

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

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

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

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

Action: For adoption of a list of outstanding issues

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

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

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

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

Action: For adoption of a list of outstanding issues

[1] Modified release formulations

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

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

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

Scope: Review of the benefit-risk balance of SGLT2 inhibitors following notification by 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 outstanding issues

3.3. Procedures for finalisation

None

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

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Enzalutamide – XTANDI (CAP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Signal of hepatotoxicity

Action: For adoption of PRAC recommendation

EPITT 18754 – New signal

Lead Member State: ES

[2] previously canagliflozin only

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

4.1.2. Nivolumab - OPDIVO (CAP); pembrolizumab –KEYTRUDA (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG (Opdivo), Merck Sharp & Dohme Limited (Keytruda)

PRAC Rapporteur: To be appointed

Scope: Signal of transplant rejection

Action: For adoption of PRAC recommendation

EPITT 18781 – New signal

Lead Member State: NL, DE

4.2. New signals detected from other sources

4.2.1. Flucloxacillin (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of acute generalised exanthematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 18773 – New signal

Lead Member State: PT

4.3. Signals follow-up and prioritisation

4.3.1. Cobicistat-containing products: cobicistat – TYBOST (CAP); cobicistat, atazanavir sulfate – EVOTAZ (CAP); cobicistat, darunavir – REZOLSTA (CAP); cobicistat elvitegravir, emtricitabine, tenofovir alafenamide – GENVOYA (CAP); cobicistat elvitegravir, emtricitabine, tenofovir disoproxil fumarate – STRIBILD (CAP); NAP

Applicants: Gilead Sciences International Ltd (Genvoya, Stribild, Tybost), Bristol-Myers Squibb Pharma EEIG (Evotaz), Janssen-Cilag International N.V. (Rezolsta)

PRAC Rapporteur: Rafe Suvarna

Scope: Signal of drug interaction with corticosteroids leading to adrenal suppression

Action: For adoption of PRAC recommendation

EPITT 18647 – Follow-up to September 2016

4.3.2. Fluoroquinolones: Ciprofloxacin (NAP); enoxacin (NAP); flumequine (NAP); levofloxacin – QUINSAIR (CAP), (NAP); lomefloxacin (NAP); moxifloxacin (NAP); norfloxacin (NAP); ofloxacin (NAP); pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP)

Applicant: Bayer, Sanofi, Raptor Pharmaceuticals Europe BV (Quinsair), various

PRAC Rapporteur: Martin Huber

Scope: Signal of uveitis

Action: For adoption of PRAC recommendation

EPITT 18686 – Follow-up to July 2016

4.3.3. Olanzapine - ZYPADHERA (CAP) - EMEA/H/C/000890/SDA/026; ZYPREXA (CAP) - EMEA/H/C/000115/SDA/047; ZYPREXA VELOTAB (CAP) - EMEA/H/C/000287/SDA/040

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of restless leg syndrome (RLS)

Action: For adoption of PRAC recommendation

EPITT 18659 – Follow-up to June 2016

4.3.4. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/SDA/003

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

Scope: Signal of increased mortality and serious adverse events (SAEs) in patients with pulmonary hypertension (PH) associated with idiopathic interstitial pneumonias (IIP) in a single clinical trial

Action: For adoption of PRAC recommendation

EPITT 18681 – Follow-up to June 2016

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Anamorelin - EMEA/H/C/003847

Scope: Treatment of anorexia, cachexia or unintended weight loss in adult patients with non-small cell lung cancer (NSCLC)

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

5.1.2. Brodalumab - EMEA/H/C/003959

Scope: Treatment of moderate to severe plaque psoriasis

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

5.1.3. Daptomycin - EMEA/H/C/004310

Scope: Treatment of complicated skin and soft-tissue infections

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

5.1.4. Etirinotecan pegol - EMEA/H/C/003874

Scope (accelerated assessment): Treatment of breast cancer with brain metastases

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

5.1.5. Methotrexate - EMEA/H/C/003756

Scope: Treatment of rheumatological and dermatological diseases

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

5.1.6. Pentosan polysulfate sodium - EMEA/H/C/004246, Orphan

Applicant: Bene-Arzneimittel GmbH

Scope: Treatment of interstitial cystitis

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

5.1.7. Rolapitant - EMEA/H/C/004196

Scope: Prevention of nausea and vomiting

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

5.1.8. Sodium zirconium cyclosilicate - EMEA/H/C/004029

Scope: Treatment of hyperkalaemia

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. Abiraterone - ZYTIGA (CAP) - EMEA/H/C/002321/II/0045

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of the RMP to modify the planned dates for assessment in the risk minimisation measures for all important identified and potential risks as well as missing information

Action: For adoption of PRAC Assessment Report

5.2.2. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0020

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Update of the RMP in order to reflect the outcome of the recently finalised procedure under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) including updates on renal impairment/renal failure; hypersensitivity and DKA. In addition, the MAH proposed to revise the dates for completion of clinical studies and included additional studies as requested in the Article 20 procedure

Action: For adoption of PRAC Assessment Report

5.2.3. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0016

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP in order to reflect the outcome of the recently finalised procedure under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) including updates on renal impairment/renal failure; hypersensitivity and DKA. In addition, the MAH proposed to revise the dates for completion of clinical studies and included additional studies as requested in the Article 20 procedure

Action: For adoption of PRAC Assessment Report

5.2.4. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS0968/0009; FORXIGA (CAP) - EMEA/H/C/002322/WS0968/0028; dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/WS0968/0012; XIGDUO (CAP) - EMEA/H/C/002672/WS0968/0023

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP in order to implement the outcome of the recently finalised procedure under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) including the addition of atypical DKA as an important identified risk for all sodium-glucose cotransporter-2 (SGLT2) inhibitors, upgrade of a drug utilisation study (DUS) from category 4 to 3 as well as the addition of a description of an ongoing mechanistic study. Finally, the RMP is updated to add a description of a DKA epidemiological study assessing the incidence of DKA

Action: For adoption of PRAC Assessment Report

5.2.5. Dronedarone - MULTAQ (CAP) - EMEA/H/C/001043/II/0035

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP to propose revised additional risk minimisation measures to facilitate healthcare professionals' (HCP) compliance and to modify the timelines for study

EFFECT-AF: a historic-prospective cohort with dynamic exposure and stratified competitive recruitment with balanced comparison groups of dronedarone versus alternative antiarrhythmic drugs of interest (EFFECT-AF/OBS13687. Annex II.D ('conditions or restrictions with regard to the safe and effective use of the medicinal product') of the Marketing Authorisation is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.6. Influenza vaccine (split virion, inactivated) - IDFLU (CAP) - EMEA/H/C/000966/WS1012/0047; INTANZA (CAP) - EMEA/H/C/000957/WS1012/0050

Applicant: Sanofi Pasteur

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the RMP (version 11.0) to include information on the enhanced safety surveillance for the Northern hemisphere (NH) 2016-2017 influenza season

Action: For adoption of PRAC Assessment Report

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

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

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

Action: For adoption of PRAC Assessment Report

5.2.8. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/II/0014

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

Scope: Revised RMP in order to add off-label use in patients with idiopathic pulmonary pneumonia, with or without pulmonary hypertension as an important identified risk

Action: For adoption of PRAC Assessment Report

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

5.3.1. 5-aminolevulinic acid - AMELUZ (CAP) - EMEA/H/C/002204/II/0024

Applicant: Biofrontera Bioscience GmbH

PRAC Rapporteur: Martin Huber

Scope: Extension of indication from 'treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2) and of field cancerization' to 'treatment

of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2) and of field cancerization in adults including the elderly; treatment of non-aggressive basal cell carcinoma (primary superficial or nodular basal cell carcinoma or mixed types of both, with good or intermediate prognosis) on the face, scalp, neck, trunk and extremities in adults including the elderly'. Consequently, sections 4.1, 4.2, 4.4, 4.6, 4.8 and 5.1 of the SmPC are updated. In addition, the MAH included some editorial changes to sections 2, 4.5, 4.7, 5.2, 6.5 and 9 of the SmPC. The Package Leaflet, Labelling and RMP (version 10) are updated accordingly. Furthermore, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)

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

5.3.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0154

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include 'adolescents from 12 years of age' to the hidradenitis suppurativa indication. As a consequence, sections 4.1, 4.2, 5.1 and 5.2, 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

5.3.3. Amifampridine - FIRDAPSE (CAP) - EMEA/H/C/001032/II/0043

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4 and 5.3 of the SmPC in order to delete the statement that amifampridine has not been fully tested in carcinogenicity models and to provide the findings from the carcinogenicity reports required for the completion of SOB 004. The RMP (version 9) is updated accordingly. In addition, the MAH took the opportunity to request the removal in Annex II of the requirement to complete carcinogenicity testing in an appropriate model

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/0026

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.4 and 4.5 of the SmPC to remove the interaction with inhibitors of breast cancer resistant protein (BCRP) based on the results of a drug-drug interaction study of the co-administration of ataluren and inhibitors of BCRP

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

5.3.5. Cabazitaxel - JEVTANA (CAP) - EMEA/H/C/002018/II/0034

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Claire Ferard

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to add information from completed study EFC11785 (randomized, open-label multicentre study comparing cabazitaxel at 20 mg/m^2 and at 25 mg/m^2 every 3 weeks in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing regimen). In addition, the MAH proposed to modify the wording in section 4.1 from 'hormone refractory' to 'castration resistant' prostate cancer to reflect the current terminology of the disease in the clinical practice. The RMP is updated accordingly and in accordance with the outcome of the latest PSUR procedure (PSUSA/000476/201506)

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

5.3.6. Carfilzomib - KYPROLIS (CAP) - EMEA/H/C/003790/II/0007/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.2 and 5.2 of the SmPC to revise the guidance on the use of carfilzomib in patients with renal and hepatic impairments further to the submission of completed studies relating to renal impairment (CFZ001: an open-label, single arm, phase 1 study of the pharmacokinetics and safety of carfilzomib in subjects with relapsed multiple myeloma and end-stage renal disease) and hepatic impairment (CFZ002: an open-label, single arm, phase 1 study of the pharmacokinetics and safety of carfilzomib in subjects with advanced malignancies and varying degrees of hepatic impairment). The RMP is updated accordingly. In addition, the MAH took the opportunity to implement some editorial changes to the Product Information

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

5.3.7. Conestat alfa - RUCONEST (CAP) - EMEA/H/C/001223/X/0034

Applicant: Pharming Group N.V

PRAC Rapporteur: Rafe Suvarna

Scope: Addition of a new pharmaceutical form 'powder and solvent for solution for injection' with self-administration kit

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

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

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

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

Tafinlar. Furthermore, the product information is brought in line with the latest QRD template (version 10)

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

5.3.9. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0052

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Update of sections 4.4 and 5.1 of the SmPC to include final results of study ICL670F2201: 'a randomized, open-label, multicentre, two-arm phase II study to evaluate the safety of deferasirox film-coated tablet (FCT) formulation and deferasirox dispersable tablet (DT) formulation in patients with transfusion dependent thalassemia or myelodysplastic syndrome (MDS) at very low, low or intermediate risk requiring chelation therapy due to iron overload' and consequent warnings (in order to fulfil ANX 047). The MAH took the opportunity to update Annex II and the RMP (version 14) are updated accordingly.

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

5.3.10. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/WS0926/0017; Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/WS0926/0016

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to include data from study 1275.9, a phase III, randomised, double-blind, parallel group, 24 week study to evaluate efficacy and safety of once daily empagliflozin 10 mg and 25 mg compared to placebo, all administered as oral fixed dose combinations with linagliptin 5 mg, in patients with type 2 diabetes mellitus and insufficient glycaemic control after 16 weeks treatment with linagliptin 5 mg once daily on metformin background therapy. In addition, the MAH took the opportunity to remove the optional sentence on 'medicinal product subject to medical prescription' from Annex IIIA. Moreover, the RMPs (version 8.0 for Jardiance; version 6.0 for Synjardy) are updated accordingly

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

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

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

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

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

5.3.12. Esomeprazole - NEXIUM CONTROL (CAP) - EMEA/H/C/002618/X/0016

Applicant: Pfizer Consumer Healthcare Ltd

PRAC Rapporteur: Simona Kudeliene

Scope: Line extension to introduce a new pharmaceutical form (gastro-resistant capsule, hard). The RMP (version 1.1) is updated accordingly

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

5.3.13. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/II/0019/G

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Rafe Suvarna

Scope: Extension of indication to include two new indications for the treatment of juvenile idiopathic arthritis and paediatric plaque psoriasis already approved for the reference medicinal product. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Annex II, the Package Leaflet, Labelling and the RMP (version 4.2) are updated accordingly. Furthermore, the product information (PI) is brought in line with the latest QRD template (version 10)

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

5.3.14. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0038

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final results of study 2993LAR-105: a randomized, open-label, multicentre, comparator-controlled study to examine the effects of exenatide long-acting release on glucose control (HbA1c) and safety in subjects with type 2 diabetes mellitus managed with diet modification and exercise and/or oral antidiabetic medications) to examine the effects of exenatide once weekly on glucose control and safety in subjects with type II diabetes mellitus

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

5.3.15. Ferric maltol - FERACCRU (CAP) - EMEA/H/C/002733/II/0002/G

Applicant: Shield TX (UK) Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of two final study reports for in vitro studies conducted as part of post-authorisation measures (MEA 001) drug-drug interaction study to investigate drug interactions with Feraccru; and (MEA 002): drug-drug interaction study to identify uridine diphosphate glucuronosyltransferase (UGT) isoenzyme(s) that are responsible for metabolism of ferric maltol. The RMP is updated accordingly

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

5.3.16. Florbetapir (^{18}F) - AMYVID (CAP) - EMEA/H/C/002422/II/0022

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to introduce quantitative read as an adjunct to visual read of florbetapir (^{18}F) positron emission tomography (PET) scans. The RMP (version 2.0) is updated accordingly. In addition, the MAH took the opportunity to bring the product information (PI) in line with the latest QRD template (version 10.0)

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

5.3.17. Indacaterol, glycopyrronium bromide - ULTIBRO BREEZHALER (CAP) - EMEA/H/C/002679/WS1005/0013; ULUNAR BREEZHALER (CAP) - EMEA/H/C/003875/WS1005/0013; XOTERNA BREEZHALER (CAP) - EMEA/H/C/003755/WS1005/0015

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of section 4.8 of the SmPC to add dysphonia and revise the adverse drug reactions selection and frequencies based on the MAH's review of all safety data. As a consequence, section 4.4 of the SmPC is updated. The Package Leaflet and the RMP (version 2.0) are updated accordingly. Annex II is updated in line with the latest QRD template

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

Applicant: Omrix Biopharmaceuticals N. V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) submission of the final results for study BIOS-13-005 (a phase III, randomized, controlled, superiority study evaluating Evarrest fibrin sealant patch versus standard of care treatment in controlling parenchymal bleeding during hepatic surgery) updating the efficacy and safety information; 2) submission of the final results for study BIOS-13-004 (a single-blinded, randomized, controlled, comparative phase III study evaluating the safety and effectiveness of Evarrest fibrin sealant patch as an adjunct to hemostasis during cardiovascular surgery) updating the efficacy and safety information; 3) submission of the final results for study 400-12-002 (a randomized, controlled, comparative phase II study evaluating the safety and effectiveness of Evarrest fibrin sealant patch as an adjunct to haemostasis during cardiovascular surgery) updating the efficacy and safety information; 4) submission of the final results for study 400-12-005 (a non-investigational post-market trial using Evarrest fibrin sealant patch as an adjunct to haemostasis in soft tissue bleeding during intra-abdominal, retroperitoneal, pelvic and non-cardiac thoracic surgery) updating the safety information; 5) update of section 5.1 of the SmPC to include further information on main existing efficacy studies. As a consequence, sections 4.8, 5.1 of the SmPC are also updated. In addition, the product information (PI) is brought in line with the latest QRD template (version 10) and Guideline on core SmPC for plasma-derived fibrin/sealant/haemostatic products (EMA/CHMP/BPWP/598816/2010 rev.1). Furthermore, section 4.2 is updated regarding the paediatric information for children under the age of 1 month, according to the EMA waiver. The RMP (version 3) is updated accordingly, including consequential and routine changes

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

5.3.20. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0025

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

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

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

5.3.21. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0027/G

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Grouped variation to: 1) update of sections 4.8 in order to include Stevens-Johnson Syndrome (SJS) and onychoclasis as post-marketing adverse drug reactions (ADRs). In addition, the MAH took the opportunity to make minor editorial amendments to the SmPC, including an editorial amendment to section 4.8 to mark the existing ADR terms of tumour lysis syndrome (added in variation EMEA/H/C/003791/II/0004), erythema, angioedema, and urticaria (added in variation EMEA/H/C/003791/0008/G) to indicate they originate from spontaneous post-marketing reports; 2) update of section 4.4 to include Hypertension as one of the risk factors for atrial fibrillation/flutter. The Package Leaflet and the RMP (version 6.2) are updated accordingly

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

5.3.22. Imiquimod - ALDARA (CAP) - EMEA/H/C/000179/II/0067

Applicant: Meda AB

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to add data on the results of study X-03016-3284 (LEIDA 2, a phase IV randomised active controlled study: long-term effects of imiquimod 5% cream and diclofenac 3% gel in the treatment of actinic keratoses on the face or scalp with respect to the risk of progression to in-situ and invasive squamous cell carcinoma) and of a meta-analysis of studies X-03016-3271 (LEIDA, a phase IV randomized active controlled study: long-term effects of imiquimod 5% cream and diclofenac 3% gel in the treatment of actinic keratoses on the face or scalp) and X-03016-3284. The RMP is updated (version 3) accordingly

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

5.3.23. Lacosamide - VIMPAT (CAP) - EMEA/H/C/000863/II/0065/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations including an extension of indication to include monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in children from 4 to less than 16 years old with epilepsy. For the treatment initiation pack, it is proposed to extend only the adjunctive treatment to adolescents weighting more than 50 kg (not suitable for monotherapy and children and adolescents weighting less than 50 kg). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 12) are updated accordingly. In addition, the MAH took the opportunity to bring Annex IIIA in line with the latest QRD template (version 10) and to introduce combined SmPC for film coated tablets. Furthermore, sections 6.3 and 6.5 of the SmPC for the syrup presentation only are updated due to the extension of shelf life of the finished product after first opening from 4 weeks to 6 months and addition of a 10 mL dosing syringe for syrup, as an additional dosing device to use in the paediatric population

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

5.3.24. Lapatinib - TYVERB (CAP) - EMEA/H/C/000795/II/0048/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations to: 1) update sections 4.4, 4.8, and 5.1 of the SmPC in order to add a warning on QTc prolongation and update safety information following the submission of study report EGF114271 (a phase IV placebo controlled single sequence crossover study to evaluate the effect of repeat oral doses of lapatinib on cardiac repolarization in patients with advanced cancer); 2) update section 4.8 of the SmPC in order to further elaborate on the undesirable effect 'serious cutaneous reactions' based on the review of the MAH's safety

database. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the product information (PI) in line with the latest QRD template (version 10) and to update Annex II to delete a condition which fulfilled with procedure ANX 28.2. The RMP (version 32) is updated accordingly also introducing template-related changes, study milestones updates, and to upgrade 'food effect' to an important identified risk (from procedure EMEA/H/C/000795/II/0024)

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

5.3.25. Ofatumumab - ARZERRA (CAP) - EMEA/H/C/001131/II/0045/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include the combination of Arzerra with fludarabine and cyclophosphamide or in combination with bendamustine for the treatment of adult patients with relapsed chronic lymphocytic leukaemia (CLL). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2, 6.6 and 9 of the SmPC are updated.The Package Leaflet and the RMP (version 13) are updated accordingly

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

5.3.26. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0009/G

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.2 and 5.2 of the SmPC to include information related to hepatic impairment based on the results of study D0816C00005 (MEA 005) (an open-label, non-randomised, multicentre, comparative, phase 1 study to determine the pharmacokinetics, safety and tolerability of olaparib following a single oral 300 mg dose to patients with advanced solid tumours and normal hepatic function or mild or moderate hepatic impairment). In addition, sections 4.4 and 4.5 are updated to include information related to moderate cytochrome P450, family 3, subfamily A (CYP3A) inducers based on the addendum to the Simcyp modelling report. The Package Leaflet and RMP are updated accordingly

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

5.3.27. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0004

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Update of section 5.2 of the SmPC to reflect the results of study 20 performed to assess the absolute bioavailability and to evaluate the pharmacokinetic (PK) parameters of osimertinib in plasma following a single oral dose and a radio-labelled intravenous (IV) microdose of [^{14}C] Tagrisso in healthy male subjects. In addition, the MAH took the opportunity to make a minor correction in SmPC section 6.5 and the Package Leaflet, where blister strips have been amended to blisters. The RMP (version 5.0) is updated accordingly

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

5.3.28. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/II/0012/G

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Grouped variations to: 1) update section 4.5 of the SmPC in order to reflect data on cytochrome P450 3A4 (CYP3A4) following submission of the results of study E1508I0242 (investigation of CYP induction potential of ospemifene at clinically relevant intestinal concentrations to exclude potential CYP3A4 induction in the intestine); 2) update of section 5.2 of the SmPC to reflect the results of study E1508I0242 (evaluation of the conversion of the Z-enantiomer of ospemifene to its E-enantiomer, evaluation of the metabolism and excretion of ospemifene and its metabolites); 3) update of section 5.2 of the SmPC to include results of studies OSP-PF-046-N and OSP-PF-047-N (in vitro investigation of plasma protein binding data of M-1 in non-clinical species for interspecies comparison between non-clinical species and humans, investigation of blood-to-plasma ratio data for ospemifene in monkey and rat and the blood-to plasma ratio for M-1 in rat, monkey and human); 4) update section 5.2 of the SmPC to reflect the results of study OSP-PF-041-N (bile salt export pump (BSEP) transporter studies post-marketing). As a consequence, the RMP (version 1.2) is updated accordingly

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

5.3.29. Panitumumab - VECTIBIX (CAP) - EMEA/H/C/000741/II/0079

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Julie Williams

Scope: Update of section 4.6 of the SmPC in order to remove references to the pregnancy surveillance programme (PSP) and lactation surveillance programmes (LSP). The Package Leaflet and the RMP are updated accordingly. In addition, the MAH took the opportunity to make further administrative updates to the RMP

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

5.3.30. Panitumumab - VECTIBIX (CAP) - EMEA/H/C/000741/II/0080

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Julie Williams

Scope: Update of Annex II in order to provide the results of biomarker analyses from the Vectibix clinical programme including study 20080763 (according to supplementary statistical analysis plan dated 20 September 2013), study 20070820 and study 20060447. The data submitted are in fulfilment of Annex II obligation ANX017. The RMP (version 21.0) is updated accordingly

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

5.3.31. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0011

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to extend the existing indication for Keytruda 50mg to include previously untreated patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumours express programmed death ligand 1 (PD-L1). As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.32. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/II/0032/G

Applicant: Ariad Pharma Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 of the SmPC based on data from ongoing study AP24534-07-101 with a median duration of follow-up of approximately 48 months for the CP-chronic myeloid leukaemia (CML) patients and 3.6 months for the advanced phase Ph+ leukaemia patients, as well as 48-month follow-up data from the ongoing study AP24534-10-201 (PACE). The Package Leaflet and the RMP (version 14.1) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and to align the annexes with the latest QRD template (version 10)

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

5.3.33. Regorafenib - STIVARGA (CAP) - EMEA/H/C/002573/II/0019

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

Scope: Update of Annex II to remove condition relating to the ceased COAST trial (study 15983: a randomized, double-blind, placebo-controlled phase-III study of adjuvant regorafenib versus placebo for patients with stage IV colorectal cancer after curative treatment of liver metastases). In addition, section 5.1 of the SmPC has been updated in order to remove information relating to KRAS mutation status and regorafenib efficacy. The RMP (version 4.2) is updated accordingly

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

5.3.34. Tadalafil - ADCIRCA (CAP) - EMEA/H/C/001021/WS0993/0025; CIALIS (CAP) - EMEA/H/C/000436/WS0993/0085

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of section 4.4 of the SmPC in order to add a new warning on the risk of non-arteritic anterior ischemic optic neuropathy (NAION) based on the final results of study H6D-MC- LVHQ (a prospective case-crossover study to evaluate the possible association

between the use of phosphodiesterase type 5 (PDE5) inhibitors and the risk of acute NAION category 3 study). The RMP (version 8.0) is updated accordingly

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

5.3.35. Tedizolid phosphate - SIVEXTRO (CAP) - EMEA/H/C/002846/II/0009

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of sections 4.4, 4.5 and 5.2 of the SmPC based on the completed drug-drug interaction study MK-1986-004 (a multiple-dose study to evaluate the effects of steady-state tedizolid phosphate administration on the pharmacokinetics and safety of a single dose of midazolam and rosuvastatin). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the annexes and to update the annexes in line with the latest QRD template (version 10). The RMP (version 2.0) is updated by removing the missing information for potential risks for drug-drug interactions mediated by CYP3A4, as well as addressing the identified risk for drug-drug interactions mediated via inhibition of breast cancer resistance protein (BCRP), adding updates made to timelines for ongoing and planned studies for long term safety and Asian population experience

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

5.3.36. Umeclidinium bromide, vilanterol - ANORO (CAP) - EMEA/H/C/002751/WS1031/0013; LAVENTAIR (CAP) - EMEA/H/C/003754/WS1031/0014

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of section 4.8 of the SmPC in order to add the adverse reactions ‘vision blurred’, ‘intraocular pressure increased’ and ‘paradoxical bronchospasm’ and to change the frequency of the adverse reaction ‘glaucoma’ from ‘not known’ to ‘rare’. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the product information (PI) in line with the latest QRD template (version 10). The RMP is updated (version 2.0) accordingly and includes revision requested as part of previous PSUSA procedures outcomes

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. Afatinib - GIOTRIF (CAP) - PSUSA/00010054/201603

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alogliptin - VIPIDIA (CAP); alogliptin, metformin - VIPDOMET (CAP); alogliptin, pioglitazone - INCRESYNC (CAP); PSUSA/00010061/201604

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Aprepitant - EMEND (CAP) - PSUSA/00000229/201603

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Canagliflozin - INVOKANA (CAP); canagliflozin, metformin - VOKANAMET (CAP) - PSUSA/00010077/201603

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Catumaxomab - REMOVAB (CAP) - PSUSA/00000581/201604

Applicant: Neovii Biotech GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Characterised viable autologous cartilage cells expanded ex vivo expressing specific marker proteins - CHONDROCELECT[4] - PSUSA/00000273/201604

Applicant: TiGenix NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For information

6.1.7. Defibrotide - DEFITELIO (CAP) - PSUSA/00010086/201604

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Dimethyl fumarate - TECFIDERA (CAP) - PSUSA/00010143/201603

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Diphtheria, tetanus, pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated), haemophilus type b conjugate vaccines (adsorbed) - HEXACIMA (CAP); HEXAXIM (Art 58[5]); HEXYON (CAP) - PSUSA/00010091/201604

Applicant: Sanofi Pasteur

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Efavirenz - STOCRIN (CAP); SUSTIVA (CAP) - PSUSA/00001200/201604 (with RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Margarida Guimarães

Scope: Evaluation of a PSUSA procedure

[4] EC decision on the MA withdrawal of ChondroCelect dated 29 July 2016

[5] 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 recommendation to CHMP

6.1.11. Empagliflozin - JARDIANCE (CAP); empagliflozin, metformin - SYNJARDY (CAP) - PSUSA/00010388/201604

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Emtricitabine - EMTRIVA (CAP) - PSUSA/00001209/201604

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Emtricitabine, tenofovir - TRUVADA (CAP) - PSUSA/00001210/201604

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Everolimus[6] - AFINITOR (CAP) - PSUSA/00010268/201603

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Exenatide - BYDUREON (CAP); BYETTA (CAP) - PSUSA/00009147/201603

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[6] Indicated for the treatment of renal cell carcinoma

6.1.16. Febuxostat - ADENURIC (CAP) - PSUSA/00001353/201604

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Fenofibrate, pravastatin - PRAVAFENIX (CAP) - PSUSA/00001363/201604

Applicant: Laboratoires SMB S.A.

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Florbetapir (^{18}F) - AMYVID (CAP) - PSUSA/00010032/201604

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Fosaprepitant - IVEMEND (CAP) - PSUSA/00001471/201603

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Histamine[7] - CEPLENE (CAP) - PSUSA/00001610/201604

Applicant: Meda AB

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Idarucizumab - PRAXBIND (CAP) - PSUSA/00010435/201604

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

[7] Indicated for treatment of acute myeloid leukaemia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Insulin degludec, liraglutide - XULTOPHY (CAP) - PSUSA/00010272/201603

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Insulin glulisine - APIDRA (CAP) - PSUSA/00001752/201604

Applicant: Sanofi-aventis Deutschland GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Ipilimumab - YERVOY (CAP) - PSUSA/00009200/201603

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Japanese encephalitis virus (inactivated) - IXIARO (CAP) - PSUSA/00001801/201603

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Macitentan - OPSUMIT (CAP) - PSUSA/00010115/201604

Applicant: Actelion Registration Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Mannitol[8] - BRONCHITOL (CAP) - PSUSA/00009226/201604

Applicant: Pharmaxis Pharmaceuticals Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Meningococcal group a, c, w135, y conjugate vaccines (conjugated to tetanus toxoid carrier protein) - NIMENRIX (CAP) - PSUSA/00010044/201604

Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Methylnaltrexone bromide - RELISTOR (CAP) - PSUSA/00002023/201603 (with RMP)

Applicant: PharmaSwiss Ceska Republika s.r.o

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Naltrexone, bupropion - MYSIMBA (CAP) - PSUSA/00010366/201603

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Netupitant, palonosetron - AKYNZEO (CAP) - PSUSA/00010393/201604

Applicant: Helsinn Birex Pharmaceuticals Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Nintedanib[9] - OFEV (CAP) - PSUSA/00010319/201604 (with RMP)

Applicant: Boehringer Ingelheim International GmbH

[8] Indicated for the treatment of cystic fibrosis
[9] Indicated for the treatment of idiopathic pulmonary fibrosis (IPF)

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Ocriplasmin - JETREA (CAP) - PSUSA/00010122/201604

Applicant: ThromboGenics NV

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Oestrogens conjugated, bazedoxifene - DUAVIVE (CAP) - PSUSA/00010321/201604

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Olanzapine pamoate - ZYPADHERA (CAP) - PSUSA/00002206/201603

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Para-aminosalicyic acid[10] - GRANUPAS (CAP) - PSUSA/00010171/201604

Applicant: Lucane Pharma

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58) – EMEA/H/W/002300/PSUV/0011

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[10] Centrally authorised product only

6.1.38. Raltegravir - ISENTRESS (CAP); lamivudine, raltegravir - DUTREBIS (CAP) - PSUSA/00010373/201603

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Regadenoson - RAPISCAN (CAP) - PSUSA/00002616/201604 (with RMP)

Applicant: Rapidscan Pharma Solutions EU Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Sofosbuvir, ledipasvir - HARVONI (CAP) - PSUSA/00010306/201604

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Margarida Guimarães

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Tacrolimus[11] - PROTOPIC (CAP) - PSUSA/00002840/201603

Applicant: Leo Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Tocilizumab - ROACTEMRA (CAP) - PSUSA/00002980/201604

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Umeclidinium bromide - INCRUSE (CAP) - PSUSA/00010263/201604

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Carmela Macchiarulo

[11] Topical formulations only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Vandetanib - CAPRELSA (CAP) - PSUSA/00009327/201604

Applicant: Genzyme Europe BV

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Vardenafil - LEVITRA (CAP); VIVANZA (CAP) - PSUSA/00003098/201603

Applicant: Bayer Pharma AG

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Vortioxetine - BRINTELLIX (CAP) - PSUSA/00010052/201603

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Zonisamide - ZONEGRAN (CAP) - PSUSA/00003152/201603

Applicant: Eisai Ltd

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Esomeprazole - NEXIUM CONTROL (CAP); NAP - PSUSA/00001269/201603

Applicant: Pfizer Consumer Healthcare Ltd (Nexium Control), various

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Hepatitis B vaccine (rDNA) - HBVAXPRO (CAP); NAP - PSUSA/00001597/201602

Applicant: Sanofi Pasteur MSD SNC (HBVaxPro), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Tenofovir - VIREAD (CAP); NAP - PSUSA/00002892/201603

Applicant: Gilead Sciences International Ltd (Viread), various

PRAC Rapporteur: Claire Ferard

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. Alprazolam (NAP) - PSUSA/00000109/201603

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Amlodipine (NAP) - PSUSA/00000174/201603

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Aprotinin (NAP) - PSUSA/00000230/201602

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Butoconazole (NAP) - PSUSA/00000471/201602

Applicant: various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Dorzolamide (NAP) - PSUSA/00003168/201602

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Dorzolamide, timolol (NAP) - PSUSA/00001166/201602

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Eletriptan (NAP) - PSUSA/00001204/201602

Applicant: various

PRAC Lead: Jana Mlada

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Ethinylestradiol, gestodene[12] (NAP) - PSUSA/00001308/201603

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Galantamine (NAP) - PSUSA/00001512/201603

Applicant: various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[12] except for transdermal application

6.3.10. Germanium (^{68}Ge) chloride, gallium (^{68}Ga) chloride (NAP) - PSUSA/00010364/201603

Applicant: various

PRAC Lead: Eva Jirsova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Gliclazide (NAP) - PSUSA/00001532/201602

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Granisetron[13] (NAP) - PSUSA/00001568/201602

Applicant: various

PRAC Lead: Tatiana Magalova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Influenza vaccine (split virion, inactivated) (NAP) - PSUSA/00010298/201603

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Influenza vaccine (split virion, inactivated, prepared in cell culture) (NAP) - PSUSA/00010299/201603

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Influenza vaccine (surface antigen, inactivated) (NAP) - PSUSA/00001744/201603

Applicant: various

[13] All formulations except transdermal patch

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Influenza vaccine (surface antigen, inactivated, adjuvanted) (NAP) - PSUSA/00010300/201603

Applicant: various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Latanoprost[14] (NAP) - PSUSA/00001834/201604

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Meningococcal group a and c polysaccharide vaccine (NAP) - PSUSA/00001970/201602

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Nicorandil (NAP) - PSUSA/00002152/201602

Applicant: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Pimecrolimus (NAP) - PSUSA/00002411/201603

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[14] Medicinal products with paediatric indication

6.3.21. Rabies vaccine (NAP) - PSUSA/00009277/201603

Applicant: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Rocuronium (NAP) - PSUSA/00002656/201602

Applicant: various

PRAC Lead: Jana Mlada

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Technetium (^{99m}Tc) pertechnetate (NAP) - PSUSA/00002866/201603

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Triamcinolone[15] (NAP) - PSUSA/00010292/201603

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Promestriene[16] (NAP) - PSUSA/00009271/201603

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and Haemophilus influenzae type b

[15] Intraocular formulations only
[16] Cream and vaginal capsules only

(Hib) conjugate vaccine (adsorbed) - INFANRIX HEXA (CAP) - EMEA/H/C/000296/LEG 116.2

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of MAH's responses to LEG 116.1 (evaluation of additional information on the recently observed increase in the reported cases of regression of psychomotor development and a cumulative review of cases in relation with lack of reconstitution following the recommendation of the PSUSA/00001122/201410 procedure dated June 2015) as per request for supplementary information (RSI) adopted in April 2016

Action: For adoption of advice to CHMP

6.4.2. Efavirenz, emtricitabine, tenofovir disoproxil - ATRIPLA (CAP) - EMEA/H/C/000797/LEG 042

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd.

PRAC Rapporteur: Martin Huber

Scope: Submission of a review of pending cases reported before conception together with a detailed analysis as requested in the recommendation of PSUSA/00001201/201507 adopted by PRAC in February 2016

Action: For adoption of advice to CHMP

6.4.3. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/LEG 071

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a detailed review on vascular death, all-cause mortality, and main vascular events observed in RIDE (a phase III randomized study of ranibizumab injection in subjects with clinically significant macular edema (ME) with center involvement secondary to diabetes mellitus) and RISE (a phase III randomized study of ranibizumab injection in subjects with clinically significant ME with center involvement secondary to diabetes mellitus) as requested in the recommendation of PSUSA/00002609/201510 adopted by PRAC in April 2016

Action: For adoption of advice to CHMP

6.4.4. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/LEG 039

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of a cumulative review on cases of liver-related events (hepatotoxicity) as requested in the recommendation of PSUSA/00002653/201509 adopted by PRAC in April 2016

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[17]

7.1.1. Cholic acid – KOLBAM (CAP) - EMEA/H/C/PSP/0017.2

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Revised PASS protocol for a patient registry to monitor the long term safety and efficacy in patients treated with cholic acid, as requested in the conclusions of EMEA/H/C/PSP/0017.1 adopted by PRAC in July 2016

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

7.1.2. Domperidone (NAP) - EMEA/H/N/PSP/j/0031.2

Applicant: Janssen (Motilium), various

PRAC Rapporteur: Claire Ferard

Scope: Revised PASS protocol for a drug utilisation study on domperidone use in Europe using databases to characterise prescribers' knowledge, understanding and extent of awareness regarding the new safety information for domperidone following the changes in the product information and the distribution of a DHPC, as requested in the conclusions of EMEA/H/N/PSP/j/0031.1 adopted by PRAC in June 2016

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[18]

7.2.1. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 017

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: PASS protocol for study ALIROC07997: 'monitoring of the safety of alirocumab in human immunodeficiency virus (HIV)-infected patients, using healthcare databases'

Action: For adoption of advice to CHMP

7.2.2. Necitumumab - PORTRAZZA (CAP) - EMEA/H/C/003886/MEA 001.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

[17] In accordance with Article 107n of Directive 2001/83/EC
[18] 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: Revised PASS protocol for a survey to assess physicians'/oncologists' understanding of the key conditions for the safe use of necitumumab, as per the request for supplementary information (RSI) adopted by PRAC and CHMP in June 2016

Action: For adoption of advice to CHMP

7.2.3. Necitumumab - PORTRAZZA (CAP) - EMEA/H/C/003886/MEA 002.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Revised PASS protocol for an observational prospective study to assess the incidence, severity, and sequelae of all serious life-threatening identified and potential risks for necitumumab treatment in the approved indication, as per the request for supplementary information (RSI) adopted by PRAC and CHMP in June 2016

Action: For adoption of advice to CHMP

7.2.4. Ocriplasmin - JETREA (CAP) - EMEA/H/C/002381/MEA 001.2

Applicant: ThromboGenics NV

PRAC Rapporteur: Julie Williams

Scope: Revised protocol for a drug utilisation study TG-MV-017 on the use of intravitreal Jetrea in clinical practice, as per the request for supplementary information (RSI) adopted by PRAC and CHMP in July 2016

Action: For adoption of advice to CHMP

7.2.5. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/MEA 093.3

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: MAH's responses to MEA 093.2 [revised PASS registry protocol for a long-term surveillance study of rituximab (Mabthera)-treated patients with granulomatosis, with polyangiitis (GPA) or microscopic polyangiitis (MPA)] as per request for supplementary information adopted in May 2016

Action: For adoption of advice to CHMP

7.2.6. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 002.1

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: MAH's response to MEA-002 [PASS protocol for study No. CLCZ696B2014: a non-interventional post-authorisation European database safety study (category 3) to characterize the risk of angioedema and other specific safety events of interest in association with use of Entresto (sacubitril/valsartan) in adult patients with heart failure] as per request for supplementary information adopted in May 2016

Action: For adoption of advice to CHMP

7.2.7. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 004.1

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: MAH's response to MEA-004 [PASS protocol for study No. CLCZ696B2015: a non-interventional post-authorisation European database safety study (category 3) to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of sacubitril/valsartan] as per request for supplementary information adopted in May 2016

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[19]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[20]

7.4.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0159

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final clinical study report (CSR) for study P06-134 entitled: 'a long-term non-interventional registry to assess safety and effectiveness of Humira in Subjects with moderately to severely active Crohn's disease' in fulfilment of MEA 056.9. The study includes also some paediatric patients and fulfils Article 46 paediatric obligations

Action: For adoption of PRAC Assessment Report

7.4.2. Aripiprazole - ABILIFY (CAP) - EMEA/H/C/000471/II/0122

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Leonor Chambel

Scope: Submission of the final clinical study report (CSR) for non-interventional, non-imposed PASS study 31-13-300 entitled: 'Abilify for the adolescent bipolar I mania indication tool effectiveness evaluation survey' to fulfil a post-authorisation measure (MEA 068.2). Annex II is updated to delete additional risk minimisation measures based on the study results and to delete PASS study 31-13-300 included by mistake during variation IB/112/G. Moreover, the RMP (version 10) is updated accordingly

Action: For adoption of PRAC Assessment Report

[19] In accordance with Article 107p-q of Directive 2001/83/EC
[20] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

7.4.3. Boceprevir - VICTRELIS (CAP) - EMEA/H/C/002332/II/0039

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Claire Ferard

Scope: Submission of the final clinical report (CSR) for a PASS study P08518 (category 3) of boceprevir among chronic hepatitis C patients entitled: 'observational prospective follow-up study to assess the utilisation of boceprevir and the management of pre-specified health outcomes of interest (HOIs) under conditions of routine clinical care'. The RMP (version 10.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0050

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Submission of the final study report for study CICL670A2301 (RMP category 3) entitled 'an international sentinel surveillance of patients with transfusional hemosideroris treated with Exjade in actual practice setting'. This submission also served to comply with Article 46 of Regulation (EC) No 1901/2006

Action: For adoption of PRAC Assessment Report

7.4.5. Nepafenac - NEVANAC (CAP) - EMEA/H/C/000818/II/0033

Applicant: Alcon Laboratories (UK) Ltd

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final study report for the drug utilisation study entitled: 'evaluation of the use of nepafenac in selected European populations' (category 3 study) to quantify and describe off-label use of nepafenac in order to fulfil MEA 012

Action: For adoption of PRAC Assessment Report

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

7.5.1. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/MEA 005.3

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reports from ARTIS (RA0021), RABBIT (RA0020), US National Databank for Rheumatic Diseases (RA0005) and BSRBR (RA0022)

Action: For adoption of advice to CHMP

7.5.2. Efavirenz, emtricitabine, tenofovir disoproxil - ATRIPLA (CAP) - EMEA/H/C/000797/MEA 039.4

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd.

PRAC Rapporteur: Martin Huber

Scope: Third annual report for malignant events associated with efavirenz: diagnostic consulting network (DCN) report as a routine risk minimisations measure

Action: For adoption of advice to CHMP

7.5.3. Everolimus - VOTUBIA (CAP) - EMEA/H/C/002311/MEA 014.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

Scope: Third interim analysis for study CRAD001MIC03 (TOSCA) a safety sub-study classified as a PASS entitled: 'international disease registry collecting data on manifestations, interventions and outcomes in patients with tuberous sclerosis complex (TSC)'

Action: For adoption of advice to CHMP

7.5.4. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 005.5

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Sixth annual report on a German registry study RABBIT: long-term observational study of the safety of biologic treatments in rheumatoid arthritis

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 005.8

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Fifth interim report of the canagliflozin independent data monitoring committee (IDMC) for the DIA3008 CANVAS study (a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus) as requested in the RMP additional pharmacovigilance activity

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 006.5

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Fourth interim report of the canagliflozin independent data monitoring committee (IDMC) for the NE-3001 CREDENCE study (a randomized, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with type 2 diabetes mellitus and diabetic nephropathy) as requested in the RMP additional pharmacovigilance activity

Action: For adoption of advice to CHMP

7.6.3. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 004.8

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Fifth interim report of the canagliflozin independent data monitoring committee (IDMC) for the DIA3008 CANVAS study (a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus) as requested in the RMP additional pharmacovigilance activity

Action: For adoption of advice to CHMP

7.6.4. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 005.5

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Fourth interim report of the canagliflozin independent data monitoring committee (IDMC) for the NE-3001 CREDENCE study (a randomized, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with type 2 diabetes mellitus and diabetic nephropathy) as requested in the RMP additional pharmacovigilance activity

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

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

Applicant: Aegerion Pharmaceuticals Limited

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Modified vaccinia Ankara virus - IMVANEX (CAP) - EMEA/H/C/002596/S/0022 (without RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Rafe Suvarna

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/S/0034 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/R/0017 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Cabozantinib - COMETRIQ (CAP) - EMEA/H/C/002640/R/0022 (without RMP)

Applicant: TMC Pharma Services Ltd

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/R/0023 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Claire Ferard

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Capecitabine - CAPECITABINE ACCORD (CAP) - EMEA/H/C/002386/R/0021 (without RMP)

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Capecitabine - CAPECITABINE TEVA (CAP) - EMEA/H/C/002362/R/0025 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Granisetron - SANCUSO (CAP) - EMEA/H/C/002296/R/0047 (without RMP)

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Jolanta Gulbinovic

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Mannitol - BRONCHITOL (CAP) - EMEA/H/C/001252/R/0028 (without RMP)

Applicant: Pharmaxis Pharmaceuticals Limited

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Meningococcal group A, C, W135 and Y conjugate vaccine - NIMENRIX (CAP) - EMEA/H/C/002226/R/0059 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Prepandemic influenza vaccine (H5N1) (whole virion, inactivated, prepared in cell culture) - VEPACEL (CAP) - EMEA/H/C/002089/R/0015 (without RMP)

Applicant: Nanotherapeutics Bohumil Sro

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Riluzole - RILUZOLE ZENTIVA (CAP) - EMEA/H/C/002622/R/0021 (without RMP)

Applicant: Aventis Pharma S.A.

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

10.3.1. Guanfacine – INTUNIV (CAP) – EMEA/H/C/003759/ANX/004

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: PRAC consultation on amendments to an imposed interventional PASS protocol for study SPD503-401: 'a comparative safety study of Intuniv in children and adolescents aged 6- 17 years with attention-deficit/hyperactivity disorder' which has been submitted in compliance with RMP version 1.5 dated 22 July 2015

Action: For adoption of advice to CHMP

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

11.2.1. Benzodiazepines: alprazolam (NAP); bromazepam (NAP); cinolazepam (NAP); clobazam (NAP); chlordiazepoxide (NAP); clotiazepam (NAP); cloxazolam (NAP); diazepam (NAP); dipotassium clorazepate (NAP); estazolam (NAP); ethyl loflazepate (NAP); etizolam (NAP); flunitrazepam (NAP); flurazepam (NAP); loprazolam (NAP); lorazepam (NAP); lormetazepam (NAP); medazepam (NAP); midazolam – BUCCOLAM (CAP), (NAP); nitrazepam (NAP); nordazepam (NAP); oxazepam (NAP); pinazepam (NAP); prazepam (NAP); quazepam (NAP); temazepam (NAP); tofisopam (NAP); triazolam (NAP); zaleplon (NAP); zopiclone (NAP); zolpidem (NAP)

Applicant: Shire Services BVBA (Buccolam), various

PRAC Lead: Julie Williams

Scope: PRAC consultation on the evaluation of a study on the impact of benzodiazepines on short-term mortality recently published in 'European Neuropsychopharmacology'

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

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

PRAC lead: Martin Huber, Rafe Suvarna, Ulla Wändel Liminga

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

12.2.1. Joint Paediatric Committee (PDCO)-PRAC Working Group – organisation of an extraordinary meeting – paediatric development and pharmacovigilance: maximising synergies

PRAC lead: Jolanta Gulbinovic

Action: For discussion

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

12.3.1. Post-authorisation efficacy study (PAES) - scientific guidance

PRAC lead: Stephen Evans, Almath Spooner

Action: For adoption

12.4. Cooperation within the EU regulatory network

12.4.1. EMA reflection paper on extrapolation across age groups - report on the multi-stakeholders extrapolation workshop

Action: For discussion

12.4.2. PRAC strategic review and learning meeting, 11-12 April 2017

PRAC lead: Amy Tanti, John Joseph Borg

Action: For discussion

12.4.3. Strengthening Collaborations for Operating Pharmacovigilance in Europe (SCOPE) - update

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. 2017 PRAC work plan – preparation

Action: For discussion

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - PRAC work tracking including quarterly workload measures and performance indicators for the last three months - predictions

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Margarida Guimarães

Action: For discussion

12.10.2. PSURs repository

None

12.10.3. Roadmap for PSUR issues: Explanatory note to 'Guideline on good pharmacovigilance practices (GVP) module VII on Periodic safety update report' - Questions & Answers (Q&A) to assessors

PRAC lead: Margarida Guimarães; Menno van der Elst

Action: For discussion

12.10.4. Roadmap for PSUR issues - Revision of the assessment report template for the evaluation of PSUSA for NAPs only

Action: For discussion

12.10.5. Union reference date (EURD) list – consultation on the draft list

Action: For adoption

12.11. Signal management

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

PRAC lead: Sabine Straus

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality - EudraVigilance auditable requirement project update - Article 57[21] reports

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.15.3. Antiretroviral Pregnancy Registry (APR) – participation of generic[22] medicinal products

PRAC lead: Rafe Suvarna

Action: For discussion

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

[21] Article 57 of Regulation (EC) No 726/2004
[22] Article 10 (1) of Directive 2001/83/EC

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public hearings - procedural and best practice guidance for PRAC members

PRAC lead: Albert van der Zeijden

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. Strategy on measuring the impact of pharmacovigilance - pilot prioritising topics relevant for collaborative impact research

PRAC lead: Marieke De Bruin

Action: For discussion

13. Any other business

14. Explanatory notes

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

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

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

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

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

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

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

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

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

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

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

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

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

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