11 January 2016
EMA/PRAC/22240/2016
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 11-14 January 2016

Chair: June Raine – Vice-Chair: Almath Spooner

11 January 2016, 13:00 – 19:00, room 3/A

12 January 2016, 08:30 – 19:00, room 3/A

13 January 2016, 08:30 – 19:00, room 3/A

14 January 2016, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

28 January 2016, 10:00 – 12:00, room 7/B, via Adobe Connect

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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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 11-14 January 2016. See (current) January 2016 PRAC minutes (to be published post February 2016 PRAC meeting).

1.2. Agenda of the meeting on 11-14 January 2016

Action: For adoption

1.3. Minutes of the previous meeting on 30 November – 3 December 2015

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. Fusafungine (NAP), nasal and oral solution - EMEA/H/A-31/1420

Applicant: Les Laboratoires Servier, various

PRAC Rapporteur: Julia Pallos; PRAC Co-rapporteur: Jana Mladá

Scope: Review of the benefit-risk balance following notification by Italy of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data
Action: For adoption of a list of experts for the Scientific Advisory Group (SAG)

3.3. Procedures for finalisation

3.3.1. Natalizumab – TYSABRI (CAP) - EMEA/H/A-20/1416

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski; PRAC Co-rapporteur: Carmela Macchiarulo

Scope: Review of the benefit-risk balance following notification by the European Commission of a referral under Article 20(8) of Regulation (EC) No 726/2004, based on pharmacovigilance data
Action: For adoption of a recommendation to CHMP

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

None

3.5. Others

None

4. Signals assessment and prioritisation[1]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Cisplatin (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of peripheral arterial thromboembolic events (ATEs) and arterial occlusion
Action: For adoption of PRAC recommendation
EPITT 18560 – New signal
Lead Member State: DK

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

4.1.2. Cytarabine – DEPOCYTE (CAP)

Applicant: Pacira Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Signal of benign intracranial hypertension
Action: For adoption of PRAC recommendation
EPITT 18533 – New signal
Lead Member State: UK

4.1.3. Dapagliflozin – FORXIGA (CAP) dapagliflozin, metformin - XIGDUO (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of pancreatitis
Action: For adoption of PRAC recommendation
EPITT 18558 – New signal
Lead Member State: SE

4.1.4. Gefitinib – IRESSA (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of pneumatosis intestinalis
Action: For adoption of PRAC recommendation
EPITT 18575 – New signal
Lead Member State: SE

4.1.5. Levetiracetam – KEPPRA (CAP)

Applicant: UCB Pharma SA

PRAC Rapporteur: Veerle Verlinden

Scope: Signal of potential medication errors due to a new presentation of syringes
Action: For adoption of PRAC recommendation
EPITT 10519 – New signal
Lead Member State: BE

4.1.6. Loratadine (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of QT prolongation and Torsade de Pointe
Action: For adoption of PRAC recommendation
EPITT 18576 – New signal
Lead Member State: BE

4.1.7. Natalizumab – TYSABRI (CAP)

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of necrotising retinitis
Action: For adoption of PRAC recommendation
EPITT 18605 – New signal
Lead Member State: DE

4.2. New signals detected from other sources

4.2.1. Quinine (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of an increased mortality risk in heart failure patients with/without concomitant use of beta-blockers
Action: For adoption of PRAC recommendation
EPITT 18529 – New signal
Lead Member State: IE

4.2.2. Warfarin (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of calciphylaxis
Action: For adoption of PRAC recommendation
EPITT 18545 – New signal
Lead Member State: DK

4.3. Signals follow-up and prioritisation

4.3.1. Methotrexate (NAP)

Applicant: various

PRAC Rapporteur: Doris Stenver

Scope: Signal of progressive multifocal leukoencephalopathy (PML) and JC[2] virus infection
Action: For adoption of PRAC recommendation
EPITT 18473 – Follow-up to September 2015

4.3.2. Oxybutynin – KENTERA (CAP) - EMEA/H/C/000532/SDA/021

Applicant: Nicobrand Limited

PRAC Rapporteur: Veerle Verlinden

Scope: Signal of psychiatric disorders

[2] John Cunningham virus (JCV)

Action: For adoption of PRAC recommendation
EPITT 18342 – Follow-up to November 2015

4.3.3. Paracetamol (NAP), phenylephrine (NAP)[3]

Applicant: various

PRAC Rapporteur: Veerle Verlinden

Scope: Signal of pharmacokinetic drug interaction increased bioavailability of phenylephrine when co-administered with paracetamol
Action: For adoption of PRAC recommendation
EPITT 18474 – Follow-up to September 2015

4.3.4. Peginterferon alfa-2a – PEGASYS (CAP) – EMEA/H/C/000395/SDA/055

Applicant: Roche Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of Guillain-Barré syndrome (GBS)
Action: For adoption of PRAC recommendation
EPITT 18402 – Follow-up to September 2015

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

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

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of inhibitor development in previously untreated patients (PUP)
Action: For adoption of PRAC recommendation
EPITT 18134 – Follow-up to May 2015

4.3.6. Saxagliptin – ONGLYZA (CAP)- EMEA/H/C/001039/SDA/0039; saxagliptin, metformin – KOMBOGLYZE (CAP) - EMEA/H/C/002059/SDA/016

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Signal of acute kidney injury
Action: For adoption of PRAC recommendation
EPITT 18379 – Follow-up to July 2015

4.3.7. Thioctic acid (NAP)

Applicant: Biologische Heilmittel Heel GmbH

PRAC Rapporteur: Marina Dimov Di Giusti

Scope: Signal of insulin autoimmune syndrome (IAS)

[3] And combination paracetamol/phenylephrine (NAP)

Action: For adoption of PRAC recommendation
EPITT 18406 – Follow-up to September 2015

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Allogeneic T cells genetically modified to express suicide gene - EMEA/H/C/002801, Orphan, ATMP[4]

Applicant: MolMed SpA

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

5.1.2. Amlodipine, valsartan - EMEA/H/C/004037

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

5.1.3. Atazanavir - EMEA/H/C/004048

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

5.1.4. Bortezomib - EMEA/H/C/004076

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

5.1.5. Daratumumab - EMEA/H/C/004077, Orphan

Applicant: Janssen-Cilag International N.V.

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

5.1.6. Eftrenonacog alfa - EMEA/H/C/004142, Orphan

Applicant: Biogen Idec Ltd

Scope: Treatment and prophylaxis of bleeding in patients with haemophilia B
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

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

5.1.8. Selexipag - EMEA/H/C/003774, Orphan

Applicant: Actelion Registration Ltd

[4] Advanced-therapy medicinal product

Scope: Treatment of pulmonary arterial hypertension (PAH)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.9. Zonisamide - EMEA/H/C/004127

Scope: Treatment of epilepsy
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. Aliskiren – RASILEZ (CAP) - EMEA/H/C/000780/WS/0771 aliskiren, hydrochlorothiazide – RASILEZ HCT (CAP) - EMEA/H/C/000964/WS/0771

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of the RMP with regard to identified risks, missing information, concomitant use of other medicines, drug-drug interactions, removal of safety issues attributed to the withdrawn aliskiren/amlodipine (Rasilamlo) and aliskiren/amlodipine/HCTZ (Rasitrio). The variation is supported by study report SPA100A: antihypertensive effects and long-term safety of aliskiren in elderly patients
Action: For adoption of PRAC AR

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

Applicant: Forest Laboratories UK Limited

PRAC Rapporteur: Rafe Suvarna

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

5.2.3. Imatinib – GLIVEC (CAP) - EMEA/H/C/000406/II/0098/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the RMP in order to exclude that there is a potential drug interactions with acetaminophen/paracetamol and imatinib, the elderly population as missing information. In addition, the RMP reflects safety actions taken since the last update including drug rash with eosinophilia and system symptoms, gastric antral vascular ectasia and chronic renal failure (from variations EMEA/H/C/000406/II/0090, II/0095 and II/0096). Finally, the due dates for the final study reports of three category 3 studies: CSTI571A2405, CSTI571A2403 and CSTI571L2401 have been amended
Action: For adoption of PRAC AR

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

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

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP with regard to the delay to start resistance monitoring, collection of off label use data, submission of reports of imposed addition pharmacovigilance activities
Action: For adoption of PRAC AR

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

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 4) and submission of a revised protocol for post authorisation safety studies (PASS) B3D-MC-GHBX[2.2] and B3D-MC-GHBX[2.3]. In addition, the RMP has been updated to include non-uraemic calciphylaxis as a potential important risk as requested by PRAC
Action: For adoption of PRAC AR

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

5.3.1. Abacavir – ZIAGEN (CAP) - EMEA/H/C/000252/WS/0845 lamivudine, abacavir – KIVEXA (CAP) - EMEA/H/C/000581/WS/0845 lamivudine, abacavir, zidovudine – TRIZIVIR (CAP) - EMEA/H/C/000338/WS/0845

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Isabelle Robine

Scope: Update of sections 4.2, 4.3, 4.4 and 5.2 of the SmPC in order to update the safety information to align the hepatic impairment wording of the following abacavir-containing products: Ziagen, Kivexa, Trizivir with the most recently approved medicinal product Triumeq. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.2. Abiraterone – ZYTIGA (CAP) - EMEA/H/C/002321/II/0036/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Grouped variation to submit clinical study reports (CSRs) associated with 4 studies listed in the RMP to address missing information in non-white patients:
1) study ABI-PRO-3001: phase 3, randomized, double-blind, placebo-pontrolled study of abiraterone acetate (JNJ-212082) plus prednisone in patients with metastatic castration-resistant prostate cancer who have failed docetaxel-based chemotherapy; 2) study 212082PCR3001: open-label study of abiraterone acetate in subjects with metastatic castration-resistant prostate cancer who have progressed after taxane-based chemotherapy; 3) study 212082PCR2007: phase 2 open-label study of abiraterone acetate (JNJ-212082) and prednisolone in patients with advanced prostate cancer who have failed androgen deprivation and docetaxel-based chemotherapy; 4) study JNJ-212082-JPN-102: phase 1 study of JNJ-212082 (abiraterone acetate) in chemotherapy-naïve patients with castration-resistant prostate cancer. In addition, submission of the interim analysis of clinical study report CSR for study ABI-PRO-3002: phase 3, randomized, double-blind,

placebo-controlled study of abiraterone acetate (JNJ-212082) plus prednisone in asymptomatic or mildly symptomatic patients with metastatic castration-resistant prostate cancer is discussed with regards to missing information for use of Zytiga in non-white patients (CSR previously submitted). The RMP (version. 11.0) is updated accordingly, including further changes from other procedures
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.3. Atazanavir, atazanavir sulfate – REYATAZ (CAP) - EMEA/H/C/000494/X/0094/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Isabelle Robine

Scope: Line extension for a new pharmaceutical form (oral powder), a new strength for the oral powder presentation (50 mg), and a new paediatric indication (patients from 3 months of age and weighing at least 5kg) grouped with an update of Reyataz capsules in light of new paediatric data. The RMP is also updated to include minor revisions with regard to nephrolithiasis folllowing PRAC's assesment of RMP version 7.3
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/0016/G

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of section 4.4 to remove precautions for use relating to the co-administration of ataluren with substrates or inducers of UGT1A9 and of section 4.5 of the SmPC to remove statements relating to the potential effect of co-administration of ataluren with inducers or substrates of UGT1A9 and to add results from studies PTC124-GD-026-HV and PTC124-GD-027-HV (MEA 011 and MEA 012). The Package Leaflet is updated accordingly. The RMP (version 4.2) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.5. Dabigatran etexilate – PRADAXA (CAP) - EMEA/H/C/000829/II/0089

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of sections 4.4 and 4.9 of the SmPC regarding the availability of the specific reversal agent for dabigatran (Praxbind (idarucizumab)). In addition, the MAH took the opportunity of this procedure to update the coagulation factors in section 4.9. The RMP (version 31.4) including the educational materials, is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.6. Deferasirox – EXJADE (CAP) - EMEA/H/C/000670/II/0045

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Corinne Féchant

Scope: Update of section 4.4 of the SmPC based on results from studies CICL670A2425, CICL670A2426 and CICL670AFR01T and patient survey. The Package Leaflet and Annex II are updated accordingly. The RMP (version 11) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.7. Deferasirox – EXJADE (CAP) - EMEA/H/C/000670/X/0043

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Corinne Féchant

Scope: Line extension for a new pharmaceutical form and new strengths (Exjade 90, 180 and 360 mg film-coated tablets)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.8. Eltrombopag – REVOLADE (CAP) - EMEA/H/C/001110/X/0022/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication to include the treatment of chronic immune (idiopathic) thrombocytopenic purpura (ITP) in paediatric (age 1 year and above) patients who had an insufficient response to other treatments (e.g. corticosteroids, immunoglobulins). Grouping with the line extension for a new tablet strength (12.5 mg) and a new powder for oral suspension formulation (25 mg)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.9. Eltrombopag – REVOLADE (CAP) - EMEA/H/C/001110/II/0029/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of sections 4.4 and 4.8 of the SmPC with reference to bone marrow reticulin formation and risk of bone marrow fibrosis and section 5.1 of the SmPC with updated exposure data, based on the final study reports for study TRA112940 (a longitudinal 2-year bone marrow study of eltrombopag olamine (SB-497115-GR) in previously treated adults, with chronic immune (idiopathic) thrombocytopenic purpura (ITP)), and study TRA105325 (EXTEND (Eltrombopag eXTENded Dosing study) an extension study of eltrombopag olamine (SB-497115-GR) in adults with chronic immune (idiopathic) thrombocytopenic purpura (ITP) previously enrolled in an eltrombopag study). As a consequence, Annex II is updated in order to delete 'increased bone marrow reticulin fibres' from the key elements to be included in the educational material.In addition, the MAH took the opportunity to propose an update of the due date in the RMP for the provision of the final clinical study report (CSR) for MEA 022.1 (effectiveness of educational materials for hepatitis C associated thrombocytopenia). The RMP (version 36) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.10. Eltrombopag – REVOLADE (CAP) - EMEA/H/C/001110/II/0030

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of sections 4.5 and 5.2 of the SmPC to reflect the drug-drug interaction with ciclosporin (RAD201583). The Package Leaflet is updated accordingly. The RMP (version 37.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.11. Human normal immunoglobulin – HYQVIA (CAP) - EMEA/H/C/002491/II/0021

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

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

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to broaden the existing indication for chronic lymphocytic leukaemia (CLL) to include all previously untreated patients including those with 17p deletion or TP53 mutation based on the results from the final clinical study report (CSR) of study PCYC-1115-CA (MEA 021). As a consequence, sections 4.1, 4.6, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP (version 5.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.13. Idelalisib – ZYDELIG (CAP) - EMEA/H/C/003843/II/0017

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of section 4.5 of the SmPC in order to amend the clinical recommendations for the co-administration of idelalisib with anticoagulants. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.14. Insulin degludec, insulin aspart – RYZODEG (CAP) - EMEA/H/C/002499/II/0017

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to include the paediatric population from 1 to 18 years of age for Ryzodeg. 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 is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.15. Insulin degludec, liraglutide – XULTOPHY (CAP) - EMEA/H/C/002647/II/0012

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to update the posology and pharmacology information in type 2 diabetes patients with moderate renal impairment
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.16. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/000717/II/0079

Applicant: Celgene Europe Limited

PRAC Rapporteur: Corinne Féchant

Scope: Extension of indication to add the treatment of adult patients with relapsed and/or refractory mantle cell lymphoma (MCL). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly. The RMP (version 25.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.17. Nintedanib – OFEV (CAP) - EMEA/H/C/003821/WS/0766; VARGATEF (CAP) - EMEA/H/C/002569/WS/0766

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Leonidas Klironomos

Scope: Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to include further information related to patients with hepatic impairment based on the clinical study reports (CSR) of studies 1199.37, 1199.39 and 1199.200. The provision of the clinical study report (CSR) of study 1199.200 addresses the post-authorisation measure MEA 001. The RMP (version 2.0) for Ofev and RMP (version 3.0) for Vargatef are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.18. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/II/0002

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment as monotherapy of locally advanced or metastatic non-squamous (NSCLC) after prior chemotherapy in adults based on study CA209057. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. Further, SmPC section 4.8 has been revised with updated combined clinical trial exposure numbers to reflect inclusion of studies in non-squamous NSCLC and in nivolumab in combination with ipilimumab in advanced melanoma. The RMP (version 3.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.19. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/II/0003

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment in combination with ipilimumab of advanced (unresectable or metastatic) melanoma in adults based on interim data from study CA209067 and the final clinical study report (CSR) of study CA209069. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been revised accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC, Annex II and Package Leaflet. The RMP (version 3.0) is updated accordingly. Paediatric non-clinical biomarker study is also provided to fulfil paediatric requirements
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.20. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/II/0008

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information on toxic epidermal necrolysis (TEN) and encephalitis. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.21. Ponatinib – ICLUSIG (CAP) - EMEA/H/C/002695/II/0028

Applicant: Ariad Pharma Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.4 and 4.8 of the SmPC with reference to renal artery stenosis. The Package Leaflet is updated accordingly. The RMP (version 13.1) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.22. Ranibizumab – LUCENTIS (CAP) - EMEA/H/C/000715/II/0059

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to reflect the information from the long-term clinical studies E2401 and E2402 in retinal vein occlusion (RVO) patients. This addresses the post-authorisation measure MEA 055. The RMP (version 15) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.23. Safinamide – XADAGO (CAP) - EMEA/H/C/002396/II/0008

Applicant: Zambon SpA

PRAC Rapporteur: Almath Spooner

Scope: Update of sections 4.5 and 5.2 of the SmPC to introduce information on on safinamide effects on breast cancer resistance protein (BCRP). The RMP is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to amend the safety information regarding the use of Olysio in interferon-free regimens, based on the primary analysis (SVR12) of studies HPC3017 and HPC3018. The Package Leaflet and Labelling are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.25. Sitagliptin – JANUVIA (CAP) - EMEA/H/C/000722/WS/0846; RISTABEN (CAP) - EMEA/H/C/001234/WS/0846; TESAVEL (CAP) - EMEA/H/C/000910/WS/0846; XELEVIA (CAP) - EMEA/H/C/000762/WS/0846

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update the safety information following completion of TECOS cardiovascular safety study. The RMP (version 6.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.26. Sitagliptin, metformin hydrochloride – EFFICIB (CAP) - EMEA/H/C/000896/WS/0847; JANUMET (CAP) - EMEA/H/C/000861/WS/0847; RISTFOR (CAP) - EMEA/H/C/001235/WS/0847; VELMETIA (CAP) - EMEA/H/C/000862/WS/0847

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update the safety information following completion of TECOS cardiovascular safety study. he RMP (version 6.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.27. Sonidegib – ODOMZO (CAP) - EMEA/H/C/002839/II/0001/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.2 and 5.2 of the SmPC to add information on posology and pharmacology of sonidegib in hepatic impaired patients resulting from study CLDE225A2113 (MEA 006) and update of section 4.5 of the SmPC to add information on drug-drug interaction with proton pump inhibitors (esomeprazole) resulting from study CLDE225A2118 (MEA 007)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.28. Telavancin – VIBATIV (CAP) - EMEA/H/C/001240/II/0023

Applicant: Clinigen Healthcare Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of section 4.2 and 5.2 of the SmPC and Annex II in order to update the guidelines for obese patients and to remove the reference to pharmacokinetic (PK) obesity study following the assessment of ANX 001.1 post authorisation measure. The Package Leaflet is updated accordingly. The RMP (version 3) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

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

5.3.30. Vemurafenib – ZELBORAF (CAP) - EMEA/H/C/002409/II/0029

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 5.1 of the SmPC in order to update the safety information with results from study (MO25653) which assessed safety and efficacy of vemurafenib in V600-mutation positive metastatic melanoma patients with previously-treated brain metastases
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.31. Vemurafenib – ZELBORAF (CAP) - EMEA/H/C/002409/II/0030

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add safety information on acute kidney injury as new adverse drug reaction with a rare frequency. The Package Leaflet and the RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.32. Vemurafenib – ZELBORAF (CAP) - EMEA/H/C/002409/II/0031/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.5 of the SmPC in order to add information on drug-drug interaction of vemurafenib with tizanidine (a CYP1A2 substrate). The RMP (version 10.0) is updated accordingly. In addition, the MAH took the opportunity to update the RMP with a proposed new due date for the final clinical study report of study GO28052 and providing RMP update for the recommendation received during procedure EMEA/H/C/002409/LEG 031 regarding agranulocytosis
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. Afamelanotide – SCENESSE (CAP) - PSUSA/10314/201506

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.2. Ambrisentan – VOLIBRIS (CAP) - PSUSA/00129/201506

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.3. Avanafil – SPEDRA (CAP) - PSUSA/10066/201506

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Miguel-Angel Macia

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.4. Azacitidine – VIDAZA (CAP) - PSUSA/00274/201505 (with RMP)

Applicant: Celgene Europe Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.5. Belatacept – NULOJIX (CAP) - PSUSA/00311/201506

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.6. Brimonidine tartrate, brinzolamide – SIMBRINZA (CAP) - PSUSA/10273/201506

Applicant: Alcon Laboratories (UK) Ltd

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.7. Bromfenac – YELLOX (CAP) - PSUSA/00436/201505

Applicant: PharmaSwiss Ceska Republika s.r.o

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.8. C1-esterase inhibitor, human – CINRYZE (CAP) - PSUSA/10104/201506

Applicant: Shire Services BVBA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.9. Cabazitaxel – JEVTANA (CAP) - PSUSA/00476/201506

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Corinne Féchant

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.10. Canakinumab – ILARIS (CAP) - PSUSA/00526/201506 (with RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.11. Daclatasvir – DAKLINZA (CAP) - PSUSA/10295/201507

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Margarida Guimarães

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.12. Dasatinib – SPRYCEL (CAP) - PSUSA/00935/201506

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.13. Dextromethorphan hydrobromide, quinidine sulfate – NUEDEXTA (CAP) - PSUSA/10089/201506

Applicant: Jenson Pharmaceutical Services Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.14. Galsulfase – NAGLAZYME (CAP) - PSUSA/01515/201505

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.15. Gefitinib – IRESSA (CAP) - PSUSA/01518/201507

Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.16. Human fibrinogen, human thrombin – EVARREST (CAP), EVICEL (CAP), RAPLIXA (CAP), TACHOSIL (CAP) - PSUSA/10297/201506

Applicant: Omrix Biopharmaceuticals N. V., ProFibrix BV, Takeda Austria GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.17. Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) – GARDASIL (CAP), SILGARD (CAP) - PSUSA/01634/201505

Applicant: Sanofi Pasteur MSD SNC, Merck Sharp & Dohme Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.18. Hydroxycarbamide – SIKLOS (CAP) - PSUSA/01692/201506 (with RMP)

Applicant: Addmedica

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.19. Imiglucerase – CEREZYME (CAP) - PSUSA/01727/201505

Applicant: Genzyme Europe BV

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.20. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP) - PSUSA/01742/201506

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.21. Liraglutide – SAXENDA (CAP), VICTOZA (CAP) - PSUSA/01892/201506

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.22. Matrix applied characterised autologous cultured chondrocytes – MACI (CAP) - PSUSA/10116/201506

Applicant: Aastrom Biosciences DK ApS

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure (MA suspension dated 19 November 2014)
Action: Adoption of recommendation to CHMP

6.1.23. Mirabegron – BETMIGA (CAP) - PSUSA/10031/201506 (with RMP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Miguel-Angel Macia

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.24. Mixture of polynuclear iron(iii)-oxyhydroxide, sucrose and starches – VELPHORO (CAP) - PSUSA/10296/201505

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.25. Nepafenac – NEVANAC (CAP) - PSUSA/02143/201505

Applicant: Alcon Laboratories (UK) Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.26. Nivolumab – NIVOLUMAB BMS (CAP), OPDIVO (CAP) - PSUSA/10379/201507

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure (Nivolumab BMS MA withdrawal dated 30 November 2015)
Action: Adoption of recommendation to CHMP

6.1.27. Nonacog gamma – RIXUBIS (CAP) - PSUSA/10320/201506

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.28. Olaparib – LYNPARZA (CAP) - PSUSA/10322/201506

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.29. Paliperidone – INVEGA (CAP), PALIPERIDONE JANSSEN (CAP), XEPLION (CAP) - PSUSA/02266/201506 (with RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.30. Pegaptanib – MACUGEN (CAP) - PSUSA/02324/201506

Applicant: PharmaSwiss Ceska Republika s.r.o

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.31. Pegloticase – KRYSTEXXA (CAP) - PSUSA/10046/201507

Applicant: Crealta Pharmaceuticals Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.32. Pertuzumab – PERJETA (CAP) - PSUSA/10125/201506

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.33. Ponatinib – ICLUSIG (CAP) - PSUSA/10128/201506 (with RMP)

Applicant: Ariad Pharma Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.34. Secukinumab – COSENTYX (CAP) - PSUSA/10341/201506

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.35. Sildenafil – REVATIO (CAP) - PSUSA/02700/201505

Applicant: Pfizer Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.36. Sofosbuvir – SOVALDI (CAP) - PSUSA/10134/201506 (with RMP)

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.37. Tobramycin – TOBI PODHALER (CAP) - PSUSA/09315/201506

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.38. Trametinib – MEKINIST (CAP) - PSUSA/10262/201505

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.39. Umeclidinium bromide, vilanterol – ANORO (CAP), LAVENTAIR (CAP) - PSUSA/10264/201506

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

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

6.2.1. Aminolevulinic acid – AMELUZ (CAP), NAP - PSUSA/10006/201506

Applicant: Biofrontera Bioscience GmbH, various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.2.2. Human normal immunoglobulin – FLEBOGAMMA DIF (CAP), HIZENTRA (CAP), HYQVIA (CAP), KIOVIG (CAP), PRIVIGEN (CAP), NAP - PSUSA/01633/201505

Applicant: Baxalta Innovations GmbH, Baxter AG, CSL Behring GmbH, Instituto Grifols S.A., various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.2.3. Imatinib – GLIVEC (CAP), NAP - PSUSA/01725/201505

Applicant: Novartis Europharm Ltd, various

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.2.4. Measles, mumps and rubella vaccine (live) – M-M-RVAXPRO (CAP), NAP - PSUSA/01937/201505

Applicant: Sanofi Pasteur MSD SNC, various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.2.5. Nevirapine – VIRAMUNE (CAP), NAP - PSUSA/02147/201505

Applicant: Boehringer Ingelheim International GmbH, various

PRAC Rapporteur: Margarida Guimarães

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.2.6. Nitric oxide – INOMAX (CAP), NAP - PSUSA/02172/201506

Applicant: Linde Healthcare AB, various

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.2.7. Olopatadine – OPATANOL (CAP), NAP - PSUSA/02211/201504

Applicant: Alcon Laboratories (UK) Ltd, various

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.2.8. Topotecan – HYCAMTIN (CAP), POTACTASOL (CAP), TOPOTECAN ACTAVIS (CAP), TOPOTECAN HOSPIRA (CAP), TOPOTECAN TEVA (CAP), NAP - PSUSA/02997/201505

Applicant: Actavis Group PTC ehf, Hospira UK Limited, Novartis Europharm Ltd, Teva B.V., various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

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

6.3.1. Apomorphine (NAP) - PSUSA/00000227/201505

Applicant: various

PRAC Lead: Doris Stenver

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

6.3.2. Bismuth subcitrate potassium, metronidazole, tetracycline (NAP) - PSUSA/00010199/201505

Applicant: various

PRAC Lead: Viola Macolić Šarinić

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

6.3.3. Ceftriaxone (NAP) - PSUSA/00000613/201505

Applicant: various

PRAC Lead: Zane Neikena

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

6.3.4. Cefuroxime sodium (for intracameral use) (NAP) - PSUSA/00010206/201505

Applicant: various

PRAC Lead: Maia Uusküla

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

6.3.5. Clevidipine (NAP) - PSUSA/00010288/201505

Applicant: various

PRAC Lead: Julie Williams

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

6.3.6. Clotiazepam (NAP) - PSUSA/00000827/201505

Applicant: various

PRAC Lead: Veerle Verlinden

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

6.3.7. Diphtheria, tetanus vaccines (adsorbed) (NAP) - PSUSA/00001128/201505

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

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

6.3.8. Fentanyl (transdermal patches, solution for injection) (NAP) - PSUSA/00001370/201504

Applicant: various

PRAC Lead: Sabine Straus

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

6.3.9. Flunarizine (NAP) - PSUSA/00001416/201505

Applicant: various

PRAC Lead: Margarida Guimarães

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

6.3.10. 5 fluorouracil, salicylic acid (NAP) - PSUSA/00000008/201505

Applicant: various

PRAC Lead: Tatiana Magalova

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

6.3.11. Gadobenic acid (NAP) - PSUSA/00001500/201504

Applicant: various

PRAC Lead: Julie Williams

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

6.3.12. Gadobutrol (NAP) - PSUSA/00001502/201504

Applicant: various

PRAC Lead: Valerie Strassmann

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

6.3.13. Gadodiamide (NAP) - PSUSA/00001503/201504

Applicant: various

PRAC Lead: Qun-Ying Yue

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

6.3.14. Gadopentetic acid (NAP) - PSUSA/00001504/201504

Applicant: various

PRAC Lead: Valerie Strassmann

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

6.3.15. Gadoteric acid (intra-articular formulation) (NAP) - PSUSA/00001505/201504

Applicant: various

PRAC Lead: Menno van der Elst

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

6.3.16. Gadoteric acid (intravenous and intravascular formulations) (NAP) - PSUSA/00001506/201504

Applicant: various

PRAC Lead: Menno van der Elst

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

6.3.17. Gadoteridol (NAP) - PSUSA/00001507/201504

Applicant: various

PRAC Lead: Doris Stenver

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

6.3.18. Gadoxetic acid disodium (NAP) - PSUSA/00001509/201504

Applicant: various

PRAC Lead: Qun-Ying Yue

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

6.3.19. Iodine (^{131}I) iobenguane (NAP) - PSUSA/00001764/201505

Applicant: various

PRAC Lead: Doris Stenver

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

6.3.20. Isotretinoin (NAP) - PSUSA/00001795/201505

Applicant: various

PRAC Lead: Julie Williams

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

6.3.21. Milnacipran (NAP) - PSUSA/00002063/201504

Applicant: various

PRAC Lead: Isabelle Robine

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

6.3.22. Misoprostol (gynaecological indication, - induction of labour) (NAP) - PSUSA/00010353/201505

Applicant: various

PRAC Lead: Doris Stenver

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

6.3.23. Misoprostol (gynaecological indication - termination of pregnancy) (NAP) - PSUSA/00010354/201505

Applicant: various

PRAC Lead: Doris Stenver

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

6.3.24. Nicergoline (NAP) - PSUSA/00002150/201505

Applicant: various

PRAC Lead: Zane Neikena

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

6.3.25. Oxaliplatin (NAP) - PSUSA/00002229/201504

Applicant: various

PRAC Lead: Corinne Féchant

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

6.3.26. Pamidronate (NAP) - PSUSA/00002269/201505

Applicant: various

PRAC Lead: Menno Van der Elst

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

6.3.27. Pholcodine (NAP) - PSUSA/00002396/201505

Applicant: various

PRAC Lead: Julie Williams

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

6.3.28. Praziquantel (NAP) - PSUSA/00002503/201504

Applicant: various

PRAC Lead: Isabelle Robine

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

6.3.29. Ranitidine (NAP) - PSUSA/00002610/201505

Applicant: various

PRAC Lead: Carmela Macchiarulo

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

6.3.30. Tafluprost (NAP) - PSUSA/00002843/201504

Applicant: various

PRAC Lead: Martin Huber

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

6.3.31. Tamoxifen (NAP) - PSUSA/00002846/201504

Applicant: various

PRAC Lead: Almath Spooner

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

6.3.32. Terlipressin (NAP) - PSUSA/00002905/201504

Applicant: various

PRAC Lead: Doris Stenver

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

6.3.33. Thiamphenicol (NAP) - PSUSA/00002925/201505

Applicant: various

PRAC Lead: Amelia Cupelli

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

6.3.34. Ticlopidine (NAP) - PSUSA/00002952/201505

Applicant: various

PRAC Lead: Amelia Cupelli

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

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Gadoversetamide – OPTIMARK (CAP) - EMEA/H/C/000745/LEG 025

Applicant: Mallinckrodt Deutschland GmbH

PRAC Rapporteur: Almath Spooner

Scope: MAH's review on data on brain accumulation: relevant literature and any other relevant data source as requested by PRAC as adopted in June 2015
Action: For adoption of advice to CHMP

6.4.2. Leflunomide – LEFLUNOMIDE MEDAC (CAP) - EMEA/H/C/001227/LEG 011

Applicant: Medac Gesellschaft fur klinische Spezialpraparate GmbH

PRAC Rapporteur: Sabine Straus

Scope: MAH's review as requested in the conclusions of EMEA/H/C/PSUSA/00001837/201409 adopted by the PRAC in April 2015
Action: For adoption of advice to CHMP

6.4.3. Omalizumab – XOLAIR (CAP) - EMEA/H/C/000606/LEG 050

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's review as requested in the conclusions of EMEA/H/C/PSUSA/00002214/201412 adopted by the PRAC in July 2015
Action: For adoption of advice to CHMP

6.4.4. Peginterferon beta-1a – PLEGRIDY (CAP) - EMEA/H/C/002827/LEG 007

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's review as requested in the conclusions of EMEA/H/C/PSUSA/00010275/201501 adopted by the PRAC in September 2015
Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

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

7.1.1. Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/PSP/0032

Applicant: Alexion Europe SAS

PRAC Rapporteur: Almath Spooner

Scope: PASS protocol for study ALX-HPP-501: an observational, longitudinal, prospective, long-term registry of patients with hypophosphatasia to collect information on the epidemiology of the disease, including clinical outcomes and quality of life, and to evaluate safety and effectiveness data in patients treated with Strensiq
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.2. Domperidone (NAP) - EMEA/H/N/PSP/j/0016.2

Applicant: Janssen (Motilium), various

PRAC Rapporteur: Isabelle Robine

Scope: Revised joint PASS protocol for a physician survey to characterise prescribers' knowledge, understanding and extent of awareness regarding the new safety information for domperidone following the change in the product information and the distribution of DHPC
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.3. Domperidone (NAP) - EMEA/H/N/PSP/j/0031

Applicant: Janssen (Motilium), various

PRAC Rapporteur: Isabelle Robine

Scope: PASS protocol for a drug utilisation study of domperidone 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 DHPC. The secondary objective of the study is to characterise the extent to which domperidone is prescribed for conditions that are not labelled
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.4. Chlormadinone acetate, ethinyl estradiol (NAP) – EMEA/H/N/PSP/j/0012.3

Applicant: Gideon Richter, various

PRAC Rapporteur: Valerie Strassmann

Scope: Revised joint PASS protocol (following conclusion of Article 31 referral procedure for combined hormonal contraceptives with CHMP opinion adopted in November 2013) to study the risk of venous thromboembolism (VTE) associated with chlormadinone/ethinylestradiol (CMA/EE)-containing products
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

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

7.1.5. Idebenone – RAXONE (CAP) - EMEA/H/C/PSP/0034

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: PASS protocol for a non-interventional study of clinical experience in patients prescribed Raxone for the treatment of Leber's hereditary optic neuropathy (LHON)
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.6. Ospemifene – SENSHIO (CAP) - EMEA/H/C/PSP/0023.2

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Revised protocol for a PASS to evaluate the incidence of venous thromboembolism and other adverse events, as agreed in the RMP, in vulvar and vaginal atrophy (VVA) patients treated with ospemifene as compared to: 1) patients newly prescribed selective oestrogen receptor modulators (SERMs) for oestrogen-deficiency conditions or breast cancer prevention; 2) the incidence in untreated VVA patients
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.7. Valproate (NAP) - EMEA/H/N/PSP/j/0029.1

Applicant: Sanofi Aventis R&D, various

PRAC Rapporteur: Sabine Straus

Scope: Revised joint PASS protocol for a drug utilisation study (DUS) to assess the effectiveness of the risk minimisation measures and to further characterise the prescribing patterns for valproate
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

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

7.2.1. Aflibercept – EYLEA (CAP) - EMEA/H/C/002392/MEA/015

Applicant: Bayer Pharma AG

PRAC Rapporteur: Isabelle Robine

Scope: PASS protocol for study 18218: assessment of the safety and drug utilisation of intravitral Eylea in real world clinical practice
Action: For adoption of advice to CHMP

7.2.2. Aflibercept – ZALTRAP (CAP) - EMEA/H/C/002532/MEA/002.3

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Revised PASS protocol for study OZONE (OBS13597) to reflect Zaltrap usage in clinical practice to address the PRAC request for supplementary information (RSI) adopted in September 2015

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

Action: For adoption of advice to CHMP

7.2.3. Agomelatine – THYMANAX (CAP) - EMEA/H/C/000916/MEA/026.1; VALDOXAN (CAP) - EMEA/H/C/000915/MEA/026.1

Applicant: Servier (Ireland) Industries Ltd., Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: MAH's response to MEA 026: revised PASS protocol for study CLE-20098-96-096: non-interventional PASS: DUS in selected European countries: a multinational, observational study to assess the effectiveness of risk-minimisation measures to address the PRAC request for supplementary information (RSI) adopted in October 2015
Action: For adoption of advice to CHMP

7.2.4. Bromelain enriched proteolytic enzyme preparation from ananas comosus – NEXOBRID (CAP) - EMEA/H/C/002246/MEA/003.3

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Valerie Strassmann

Scope: Revised PASS protocol for study MW2013-06-01: drug utilisation study (DUS) to further evaluate the effectiveness of the risk minimisation activities (including evaluation of educational and training materials): MAH's responses to MEA 03.2 request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.2.5. Buprenorphine, naloxone – SUBOXONE (CAP) - EMEA/H/C/000697/MEA/023.5

Applicant: Indivior UK Limited

PRAC Rapporteur: Martin Huber

Scope: Revised protocol for PASS study PE-US-005: suboxone mortality study in the UK with the Health Improvement Network database (THIN): MAH's responses to MEA 023.4 request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.2.6. Cobicistat – TYBOST (CAP) - EMEA/H/C/002572/MEA/012.2

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: MAH's responses to MEA 012.2 request for supplementary information (RSI) as adopted by PRAC in December 2014: request for a waiver for study GS-EU-216-1230: prospective, observational drug utilisation study of cobicistat in adults with human immunodeficiency virus (HIV)-1 infection due to feasibility related issues
Action: For adoption of advice to CHMP

7.2.7. Collagenase clostridium histolyticum – XIAPEX (CAP) - EMEA/H/C/002048/MEA/027.1

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 027 [PASS protocol for a non-interventional survey to evaluate the effectiveness of Xiapex educational material for healthcare professionals in the treatment of Peyronie's disease] to address the PRAC request for supplementary information (RSI) as adopted in July 2015
Action: For adoption of advice to CHMP

7.2.8. Filgrastim – NIVESTIM (CAP) - EMEA/H/C/001142/MEA/015

Applicant: Hospira UK Limited

PRAC Rapporteur: Kirsti Villikka

Scope: PASS protocol for study ZOB-NIV-1513: a multinational, multicentre, prospective, non-interventional, post-authorisation safety study in healthy donors (HDs) exposed to Nivestim for haematopoietic stem cell (HSC) mobilisation (NEST)
Action: For adoption of advice to CHMP

7.2.9. Flutemetamol (^{18}F) – VIZAMYL (CAP) - EMEA/H/C/002557/MEA/003.2

Applicant: GE Healthcare Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 003.1 request for supplementary information (RSI) adopted by PRAC in September 2015:revised PASS protocol for a drug utilisation study as an additional pharmacovigilance activity to further characterize the safety concern (GE067-028)
Action: For adoption of advice to CHMP

7.2.10. Human normal immunoglobulin – PRIVIGEN (CAP) - EMEA/H/C/000831/MEA/022.3

Applicant: CSL Behring GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 022.1 : revised protocol for study IgPro10_5003 (updated version 2.0): an observational hospital-based cohort study in the US: Privigen use and haemolytic anaemia in adults and children and the Privigen safety profile in children with chronic inflammatory demyelinating polyneuropathy (CIDP)
Action: For adoption of advice to CHMP

7.2.11. Ibrutinib – IMBRUVICA (CAP) - EMEA/H/C/003791/MEA/023.2

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 023.2 [PASS protocol study PCYC-PMR-2060-04] as adopted in September 2015: enhanced pharmacovigilance to evaluate the risks of haemorrhage with the administration of ibrutinib
Action: For adoption of advice to CHMP

7.2.12. Meningococcal group b vaccine (rDNA, component, adsorbed) – BEXSERO (CAP) - EMEA/H/C/002333/MEA/017

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: Revised PASS protocol for study V72_36OB: a post-licensure observational safety study after meningococcal B vaccine 4CMenB (Bexsero) vaccination in routine UK care
Action: For adoption of advice to CHMP

7.2.13. Safinamide – XADAGO (CAP) - EMEA/H/C/002396/MEA/004

Applicant: Zambon SpA

PRAC Rapporteur: Almath Spooner

Scope: Protocol for study Z7219N02, a drug utilisation study (DUS): observational European multicentre retrospective-prospective cohort study to observe Safinamide safety profile and pattern of use in clinical practice during the first post-commercialisation phase
Action: For adoption of advice to CHMP

7.2.14. Sofosbuvir – SOVALDI (CAP) - EMEA/H/C/002798/MEA/021

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Protocol for study GS-EU-337-2030: observational, cross-sectional post-authorisation safety study to assess healthcare providers awareness of risks related to sofosbuvir and ledipasvir/sofosbuvir (LDV/SOF)
Action: For adoption of advice to CHMP

7.2.15. Sofosbuvir, ledipasvir – HARVONI (CAP) - EMEA/H/C/003850/MEA/013.1

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Margarida Guimarães

Scope: Revised protocol for study GS-EU-337-1820: prospective observational drug utilisation study (DUS) of ledipasvir/sofosbuvir (LDV/SOF) in adults with hepatitis C (HCV)/human immunodeficiency virus (HIV) co-infection
Action: For adoption of advice to CHMP

7.2.16. Sofosbuvir, ledipasvir – HARVONI (CAP) - EMEA/H/C/003850/MEA/014

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Margarida Guimarães

Scope: Protocol for study GS-EU-337-2030: observational, cross-sectional PASS to assess healthcare providers awareness of risks related to sofosbuvir and ledipasvir/sofosbuvir (LDV/SOF)
Action: For adoption of advice to CHMP

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

None

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

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

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

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Isabelle Robine

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

7.4.2. Aliskiren – RASILEZ (CAP) - EMEA/H/C/000780/WS/0807 aliskiren, hydrochlorothiazide – RASILEZ HCT (CAP) - EMEA/H/C/000964/WS/0807 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Submission of final results of the non-interventional (NIS) aliskiren study SPP100A2418 (or A2413) on the incidence of colorectal hyperplasia and gastrointestinal cancer in aliskiren treated patients
Action: For adoption of PRAC Assessment Report

7.4.3. Catridecacog – NOVOTHIRTEEN (CAP) - EMEA/H/C/002284/II/0012/G

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Isabelle Robine

Scope: Update of the RMP to include exposure and safety data following finalisation of clinical trial F13CD-3835 (evaluation of long term safety of monthly replacement therapy with recombinant factor XIII when used for prevention of bleeding episodes in paediatric subjects with congenital factor XIII A-subunit deficiency). In addition, inclusion of the final study report of PRO-RBDD registry (prospective data collection on congenital factor XIII deficiency)
Action: For adoption of PRAC AR

7.4.4. Eptacog alfa – NOVOSEVEN (CAP) - EMEA/H/C/000074/II/0089 (with RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Sabine Straus

[8] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013
[9] Article 58 of Regulation (EC) No 726/2004 allows the Agency's Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO), on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

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

7.4.5. Panitumumab – VECTIBIX (CAP) - EMEA/H/C/000741/II/0073 (with RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Julie Williams

Scope: Submission of the final study report for study 20101120, a category 3 study assesing the impact of the RAS test results on patterns of panitumumab use, intended to measure the effectiveness of the risk minimisation measures for Vectibix. The RMP (version 18.0) is updated accordingly
Action: For adoption of PRAC Assessment Report

7.4.6. Telaprevir – INCIVO (CAP) - EMEA/H/C/002313/II/0039

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final results for study VX-950HPC4004: drug utilisation study (DUS) of Incivo (telaprevir) in Europe: adherence to virologic stopping rules and use in patient subgroups as required pharmacovigilance activity (category 3) in the RMP
Action: For adoption of PRAC Assessment Report

7.4.7. Vildagliptin – GALVUS (CAP) - EMEA/H/C/000771/WS/0791, JALRA (CAP) - EMEA/H/C/001048/WS/0791, XILIARX (CAP) - EMEA/H/C/001051/WS/0791 Vildagliptin / metformin hydrochloride – EUCREAS (CAP) - EMEA/H/C/000807/WS/0791, ICANDRA (CAP) - EMEA/H/C/001050/WS/0791, ZOMARIST (CAP) - EMEA/H/C/001049/WS/0791 (with RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final results of PASS study CLAF237A2401 and a revised RMP (version 13.0) to add the study information and to include rhabdomyolysis under the current potential risk as muscle events/myopathy/rhabdomyolysis, in particular with concurrent statin use following the PSUSA/00003113/201502 PRAC recommendation on a signal of rhabdomyolysis with the use of vildagliptin containing products
Action: For adoption of PRAC Assessment Report

7.5. Interim results of imposed and non-imposed PASS submitted before the entry into force of the revised variation regulation[10]

7.5.1. Indacaterol, glycopyrronium bromide – ULTIBRO BREEZHALER (CAP) - EMEA/H/C/002679/MEA/003.3

Applicant: Novartis Europharm Ltd

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

PRAC Rapporteur: Torbjorn Callreus

Scope: MAH's responses to MEA 003.2 request for supplementary information (RSI) as adopted in October 2015: first interim report for a drug utilisation study CQVA 149A2401
Action: For adoption of advice to CHMP

7.5.2. Indacaterol, glycopyrronium bromide – ULUNAR BREEZHALER (CAP) - EMEA/H/C/003875/MEA/004.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: MAH's responses to MEA 004.1 request for supplementary information (RSI) as adopted in October 2015: first interim report for a drug utilisation study CQVA 149A2401
Action: For adoption of advice to CHMP

7.5.3. Indacaterol, glycopyrronium bromide – XOTERNA BREEZHALER (CAP) - EMEA/H/C/003755/MEA/003.3

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: MAH's responses to MEA 003.2 request for supplementary information (RSI) as adopted in October 2015: first interim report for a drug utilisation study (DUS) CQVA 149A2401
Action: For adoption of advice to CHMP

7.5.4. Infliximab – REMICADE (CAP) - EMEA/H/C/000240/MEA/089.12

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim study reports for the EU rheumatoid arthritis registries: ARTIS and RABBIT cohort 2, ENCORE patient registry in Europe in Crohn's disease
Action: For adoption of advice to CHMP

7.5.5. Infliximab – REMICADE (CAP) - EMEA/H/C/000240/MEA/121.8

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim annual report for study P04808 on the adult ulcerative colitis (UC) patient registry (OPUS), including the investigation of episodic/re-treatment
Action: For adoption of advice to CHMP

7.5.6. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA/004.4

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Interim results of the enhanced safety surveillance study D2560C00008: a postmarketing non-interventional cohort study of the safety of live attenuated influenza vaccine (LAIV) in subjects 2 through 17 years of age
Action: For adoption of advice to CHMP

7.5.7. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA/006.3

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Second annual report for study MI-MA194: a post-marketing observational evaluation of the safety of Fluenz Tetra in children and adolescents with high-risk conditions
Action: For adoption of advice to CHMP

7.5.8. Influenza vaccine (split virion, inactivated) – IDFLU (CAP) - EMEA/H/C/000966/MEA/032.2; INTANZA (CAP) - EMEA/H/C/000957/MEA/032.2

Applicant: Sanofi Pasteur (IDflu), Sanofi Pasteur MSD SNC (Intanza)

PRAC Rapporteur: Miguel-Angel Macia

Scope: Interim results of the enhanced passive safety surveillance for 2015-2016 campaign
Action: For adoption of advice to CHMP

7.5.9. Nomegestrol, estradiol – ZOELY (CAP) - EMEA/H/C/001213/ANX/011.1

Applicant: Teva B.V.

PRAC Rapporteur: Corinne Féchant

Scope: PASS interim results for a prospective observational study (ZEG2013_08) to assess the risk of venous thromboembolic events (VTE) and arterial thromboembolic events (ATE) in nomegestrel / estradiol users compared with the VTE risk in users of combined oral contraceptives containing levonorgestrel (as imposed in accordance with Article 10(a) of Regulation (EC) No. 726/2004)
Action: For adoption of advice to CHMP

7.5.10. Temsirolimus – TORISEL (CAP) - EMEA/H/C/000799/LEG/031.3

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Interim results from Japanese non-interventional studies 3066K5-4406 (Torisel 25 mg for intravenous drip infusion special investigation - all patients survey) and B1771016 (Torisel 25 mg for intravenous drip infusion special investigation - survey on long term use)
Action: For adoption of advice to CHMP

7.5.11. Tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/MEA/256.5

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Isabelle Robine

Scope: MAH's responses to MEA 256.4 request for supplementary information (RSI) as adopted in September 2015: interim results for a drug utilisation study (DUS), study GS-

EU-174-0224 in human immunodeficiency virus (HIV)-1 and hepatitis B virus (HBV)-infected paediatric patients to follow-up the effectiveness of the risk minimisation measures
Action: For adoption of advice to CHMP

7.5.12. Tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/MEA/272

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Interim report for study GS-DE-174-0225: prospective assessment of the real-life treatment outcomes of six years of Viread in chronic hepatitis B (CHB) following-up on the German multicentre non-interventional study (GEMINIS): VIR-Life
Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Rivastigmine – EXELON (CAP) - EMEA/H/C/000169/MEA 036.1, PROMETAX (CAP) - EMEA/H/C/000255/MEA 037.1

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Fourth 6-monthly interim report on the trends of multiple patch use and with Council for International Organizations of Medical Sciences (CIOMS) reports of medication errors and misuse (01 February-2015 to 31 July2015)
Action: For adoption of advice to CHMP

7.7. New Scientific Advice

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

7.8. Ongoing Scientific Advice

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

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

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

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Mecasermin – INCRELEX (CAP) - EMEA/H/C/000704/S/0035 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Annual reassessment of the marketing authorisation
Action: For adoption of advice to CHMP

8.1.2. Tafamidis – VYNDAQUEL (CAP) - EMEA/H/C/002294/S/0031 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Isabelle Robine

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. Ceritinib – ZYKADIA (CAP) - EMEA/H/C/003819/R/0004 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

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

8.2.2. Delamanid – DELTYBA (CAP) - EMEA/H/C/002552/R/0010 (without RMP)

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Rafe Suvarna

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

8.2.3. Pixantrone dimaleate – PIXUVRI (CAP) - EMEA/H/C/002055/R/0025 (with RMP)

Applicant: CTI Life Sciences Limited

PRAC Rapporteur: Rafe Suvarna

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

8.3. Renewals of the marketing authorisation

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

Applicant: Shire Services BVBA

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

8.3.2. Denosumab – XGEVA (CAP) - EMEA/H/C/002173/R/0042 (with RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

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

8.3.3. Ipilimumab – YERVOY (CAP) - EMEA/H/C/002213/R/0035 (with RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

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

8.3.4. Linagliptin – TRAJENTA (CAP) - EMEA/H/C/002110/R/0021 (without RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

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

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

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

10.1. Safety related variations of the marketing authorisation

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

emtricitabine, tenofovir disoproxil – TRUVADA (CAP) - EMEA/H/C/000594/WS/0792 tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/WS/0792

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

PRAC Rapporteur: Rafe Suvarna

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

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

None

10.3. Other requests

10.3.1. Human thrombin[11] – FLOSEAL HEMOSTATIC MATRIX (FLOSEAL V/H SD[12]) (medical device); HEMOBLAST HAEMOSTATIC AGENT (medical device); SURGIFLO HAEMOSTATIC MATRIX KIT (medical device)

Applicant: Baxter AG; Biom' Up; Ferrosan A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: PRAC consultation on the potential applicability of the recommendation of the signal of intestinal obstruction with human fibrinogen/human thrombin (TachoSil) (EPITT 18373) to Floseal V/H SD; Hemoblast Haemostatic Agent; Surgiflo Haemostatic Matrix Kit
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

11.1.1. Cyproterone acetate, ethinylestradiol (NAP) - NL/H/xxxx/WS/150

Applicant: Bayer (Diane-35 and generics)

PRAC Lead: Menno van der Elst

Scope: PRAC consultation on a variation procedure evaluating the first interim report of the joint database drug utilisation study (DUS) on the use of cyproterone acetate/ethinylestradiol (CPA/EE) and based on the protocol approved by the PRAC in April 2015, as per the conclusions of the referral procedure under Art 107i of Directive 2001/83/EC (EMEA/H/A-107i/1357) finalised in 2013
Action: For adoption of advice to Member States

[11] As an ancillary medicinal substance
[12] Vapor heated, solvent/detergent treated

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh

12.2.1. Joint Paediatric Committee (PDCO)-PRAC Working Group - guideline on conduct of pharmacovigilance for medicines used by the paediatric population

PRAC lead: Jolanta Gulbinovič; Amy Tanti
Action: For adoption

12.2.2. Paediatric Committee (PDCO) - paediatric pharmacovigilance: organ maturation tables

Action: For discussion

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

12.3.1. Advisory group on classification of post-authorisation studies (CPAS) to the marketing authorisations

Action: For discussion

12.3.2. Guideline on safety and efficacy follow-up – risk management plan of ATMPs

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. EMA review of seasonal influenza vaccines enhanced safety surveillance systems

Action: For discussion

12.4.2. EMA reflection paper on extrapolation across age groups

PRAC lead: Jolanta Gulbinovič
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. PRAC work plan 2016

Action: For adoption

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

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

12.10.3. PSUR action group - roadmap for PSUR issues: scoping paper as a basis for the workshop in January 2016

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

12.10.4. PSUR/PSUSA – guidance on handling of EU single PSUR procedures for suspended or withdrawn/non-renewed/revoked marketing authorisations

Action: For discussion

12.10.5. PSURs repository – update on post-audit requirements

Action: For discussion

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

Action: For adoption of the revised list

12.11. Signal management

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

PRAC lead: Sabine Straus

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

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

Action: For adoption

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems - Summaries of risk management plans (RMP): update

Action: For discussion

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Initial marketing authorisation(s) - revised accelerated assessment procedural timetables

PRAC lead: Ulla Wändel Liminga
Action: For adoption

12.20.2. Pharmacovigilance operation and implementation - proposal for a streamlined governance structure

Action: For discussion

12.20.3. Strategy on impact of pharmacovigilance

Action: For adoption

13. Any other business

None

14. Explanatory notes

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

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

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

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

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

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

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

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

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

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

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

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

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

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