30 November 2015
EMA/PRAC/808595/2015
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 30 November – 3 December 2015

Chair: June Raine – Vice-Chair: Almath Spooner

30 November 2015, 13:00 – 19:00, room 3/A

01 December 2015, 08:30 – 19:00, room 3/A

02 December, 08:30 – 19:00, room 3/A

03 December, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

17 December 2015, 10:00 – 12:00, room 6/B, via teleconference

Health and safety information

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

Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure 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 30 November-3 December 2015. See December 2015 PRAC minutes (to be published post January 2016 PRAC meeting).

1.2. Adoption of agenda of the meeting of 30 November-3 December 2015

1.3. Adoption of the minutes of the previous meeting on 3-6 November 2015

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 outstanding issues

3.2.2. 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 list of outstanding issues

3.3. Procedures for finalisation

None

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. Adalimumab – HUMIRA (CAP)

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of glomerulonephritis (GN)
Action: For adoption of PRAC recommendation

[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

EPITT 18528 – New signal
Lead Member State(s): SE

4.1.2. Dabigatran – PRADAXA (CAP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Signal of pulmonary alveolar haemorrhage
Action: For adoption of PRAC recommendation
EPITT 18516 – New signal
Lead Member State(s): DK

4.1.3. Flucloxacillin (NAP); paracetamol (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of metabolic acidosis following administration of flucloxacillin in association with paracetamol
Action: For adoption of PRAC recommendation
EPITT 18514 – New signal
Lead Member State(s): PT

4.1.4. Infliximab – INFLECTRA (CAP), REMICADE (CAP), REMSIMA (CAP)

Applicant: Hospira UK Limited (Inflectra), Janssen Biologics B.V. (Remicade), Celltrion Healthcare Hungary Kft. (Remsima)

PRAC Rapporteur: To be appointed

Scope: Signal of thyroid gland disorders
Action: For adoption of PRAC recommendation
EPITT 18530 – New signal
Lead Member State(s): SE, UK

4.1.5. Olanzapine –ZYPADHERA (CAP), ZYPREXA (CAP), ZYPREXA VELOTAB (CAP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)
Action: For adoption of PRAC recommendation
EPITT 18534 – New signal
Lead Member State(s): FI

4.1.6. Vismodegib - ERIVEDGE (CAP)

Applicant: Roche Registration Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of angioedema

Action: For adoption of PRAC recommendation
EPITT 18526 – New signal
Lead Member State(s): SE

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Hormone replacement therapy medicinal products containing oestrogens or oestrogens and progestogens in combination (NAP); bazedoxifene, oestrogens conjugated – DUAVIVE (CAP)

Applicant: Pfizer Limited (Duavive), various

PRAC Rapporteur: Menno van der Elst

Scope: Signal of increased risk of ovarian cancer
Action: For adoption of PRAC recommendation
EPITT 18258 – Follow-up to September 2015

4.3.2. Human fibrinogen, human thrombin – TACHOSIL (CAP) - EMEA/H/C/000505/SDA/041

Applicant: Takeda Austria GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of intestinal obstruction
Action: For adoption of PRAC recommendation
EPITT 18373 – Follow-up to November 2015

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Caspofungin - EMEA/H/C/004134

Generic

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

5.1.2. Daclizumab - EMEA/H/C/003862

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

5.1.3. Dexamethasone - EMEA/H/C/004071, Orphan

Applicant: Laboratoires CTRS, Hybrid

Scope: Treatment of symptomatic multiple myeloma in combination with other medicinal products
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.4. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982

Scope: Vaccination against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and invasive diseases caused by Haemophilus influenzae type b (Hib)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.5. Emtricitabine, tenofovir alafenamide - EMEA/H/C/004094

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

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

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

5.1.7. Infliximab - EMEA/H/C/004020

Biosimilar

Scope: Treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.8. Ixazomib - EMEA/H/C/003844

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

5.1.9. Ixekizumab - EMEA/H/C/003943

Scope: Treatment of moderate to severe plaque psoriasis
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.10. Lesinurad - EMEA/H/C/003932

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

5.1.11. Necitumumab - EMEA/H/C/003886

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

5.1.12. Rasagiline - EMEA/H/C/004064

Generic

Scope: Treatment of idiopathic Parkinson's disease (PD)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.13. Rociletinib - EMEA/H/C/004053

Scope: Treatment of patients with mutant epidermal growth factor receptor (EGFR) non-small cell lung cancer (NSCLC)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Actelion Registration Ltd

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

5.1.15. Sirolimus - EMEA/H/C/003978 - Orphan

Applicant: Santen Oy

Scope: Treatment of chronic non-infectious uveitis
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.16. Trifluridine, tipiracil - EMEA/H/C/003897

Scope: Treatment of colorectal cancer
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. Oseltamivir – TAMIFLU (CAP) - EMEA/H/C/000402/II/0114

Applicant: Roche Registration Ltd

PRAC Rapporteur: Kirsti Villikka

Scope: Proposal for a new and alternative study BV29684 'assessing the safety of prenatal exposure to oseltamivir' as category 3 study (MEA 099) to replace the agreed 2-year extension of the Danish-Swedish registry (NV25577)
Action: For adoption of PRAC AR

5.2.2. Turoctocog alfa – NOVOEIGHT (CAP) - EMEA/H/C/002719/II/0011/G

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Revised RMP edition 3 version 1 to include criteria of category 3 study NN7008-3553 PASS, due date for the provision of the final clinical study report (CSR) for study NN7008-

3553. In addition, information on ongoing PASS study in Japan NN7008-4105 has been added; clinical trial NN7008-3568 has been removed
Action: For adoption of PRAC AR

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

5.3.1. Abatacept – ORENCIA (CAP) - EMEA/H/C/000701/II/0089

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Update of section 4.6 of the SmPC in order to update the safety information on the risk of infection associated with live vaccination in infants born to women treated with abatacept during pregnancy. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variation to amend sections 4.8 and 5.1 of the SmPC in order to update the safety information with data from the long-term (LT) final clinical study report for IM101174.In addition, the timelines for study IM101537, aimed at evaluating the effectiveness of risk minimisation measure (alert card) are updated
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.3. Adalimumab – HUMIRA (CAP) - EMEA/H/C/000481/II/0146

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of non-infectious intermediate, posterior and panuveitis in adult patients. 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

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

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

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

5.3.5. Ataluren – TRANSLARNA (CAP) - EMEA/H/C/002720/II/0012

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of cystic fibrosis resulting from a nonsense mutation in at least one allele of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Consequently, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.6. Conestat alfa – RUCONEST (CAP) - EMEA/H/C/001223/II/0032

Applicant: Pharming Group N.V

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to remove the requirement for testing all new patients for immunoglobulin E (IgE) antibodies against rabbit epithelium (dander) prior to initiation of treatment and the requirement for repeat testing of IgE antibodies to rabbit dander. The Package Leaflet is updated accordingly. The Annex II is updated to reflect changes to the educational material. The RMP is also updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.7. Dabigatran etexilate – PRADAXA (CAP) - EMEA/H/C/000829/II/0085

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of sections 4.2 and 5.1 of the SmPC to add the recommendation that Pradaxa should be taken with a meal and/or a proton pump inhibitor such a pantoprazole in case of gastrointestinal symptoms (GIS), based on the results of study 1160.128 'a prospective, open label study evaluating the efficacy of two management strategies on gastrointestinal symptoms (GIS) in non-valvular atrial fibrillation (NVAF) patients'. The Package Leaflet (including the patient alert card) is updated accordingly. The RMP (version 31.2) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

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

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

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final study report of the clinical study GS-US-236-0118: Phase 3 open-label safety study of COBI-containing highly active ARV regimens in HIV-1 infected

patients with mild to moderate renal impairment (category 3 study in the RMP) in order to update the relevant information on the RMP
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.5 of the SmPC in order to update the safety information with the potential drug interaction of ledipasvir/sofosbuvir (LDV/SOF), as well as that of LDV and SOF as single agents with tenofovir disoproxil fumarate (TDF). The Package Leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.11. Efavirenz, emtricitabine, tenofovir disoproxil – ATRIPLA (CAP) - EMEA/H/C/000797/WS/0829; emtricitabine, rilpivirine, tenofovir disoproxil – EVIPLERA (CAP) - EMEA/H/C/002312/WS/0829; emtricitabine, tenofovir disoproxil – TRUVADA (CAP) - EMEA/H/C/000594/WS/0829; tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/WS/0829

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

PRAC Rapporteur: Isabelle Robine

Scope: Update of section 4.5 of the Viread, Truvada, Atripla and Eviplera SmPCs regarding potential drug interaction of ledipasvir/sofosbuvir (LDV/SOF) as well asthat of LDV and SOF as single agents with tenofovir disoproxil fumarate. The RMP is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.12. Fentanyl – INSTANYL (CAP) - EMEA/H/C/000959/X/0030/G

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Isabelle Robine

Scope: Grouped variation to replace the current multi-dose nasal spray by a new improved child resistant multi-dose nasal spray. Addition of a new packsize of 30 doses for each current strength (50 micrograms/dose, 100 micrograms/dose and 200 micrograms/dose). Tightening of the assay release limit of the multi-dose finished product to 98.0%-102.0%. Reduction of the shelf life for all strengths of the multi-dose finished product to 24 months. Additionally, the MAH took the opportunity to include an editorial change, to change the wording of the specification footnote regarding the droplet size distribution test
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/0011

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Extension of indication to include the combination of idelalisib with ofatumumab. As a consequence, sections 4.1, 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

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

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Qun-Ying Yue

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

5.3.15. Lixisenatide – LYXUMIA (CAP) - EMEA/H/C/002445/II/0014

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the safety information on older patients with type 2 diabetes mellitus inadequately controlled on their current diabetes treatment regimen and on patients with renal impairment following submission of study EFC12703 in fulfilment of MEA 006
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.16. Lomitapide – LOJUXTA (CAP) - EMEA/H/C/002578/X/0016

Applicant: Aegerion Pharmaceuticals

PRAC Rapporteur: Menno van der Elst

Scope: Application for a line extension to include 30 mg, 40 mg and 60 mg hard capsules.
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.17. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/II/0004

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

5.3.18. Obinutuzumab – GAZYVARO (CAP) - EMEA/H/C/002799/II/0007

Applicant: Roche Registration Ltd

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to add the treatment of patients with follicular lymphoma based on the results of the pivotal study GAO4753g. Consequently, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC are udpated. The Package Leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.19. Oritavancin – ORBACTIV (CAP) - EMEA/H/C/003785/II/0003

Applicant: The Medicines Company UK Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of sections 4.3, 4.4 and 4.5 of the SmPC in order to include information on the interaction potential between oritavancin and phospholipid-dependent and phospholipid-independent laboratory coagulation tests following the conclusion of two RMP category 3 studies. The Package Leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

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

5.3.21. Pazopanib – VOTRIENT (CAP) - EMEA/H/C/001141/II/0032/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Grouped variation to amend section 5.3 of the SmPC in order to update the safety information following completion of two carcinogenicity studies in mice and rats. In addition, the MAH submitted a study on the induction of cytochrome P450 (CYP) mRNA expression in mice. Moreover, the RMP (version 15) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.22. Pazopanib – VOTRIENT (CAP) - EMEA/H/C/001141/II/0033

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Update of section 4.4 and 5.1 of the SmPC in order to update pharmacogenomics information following the results of a meta-data analysis (study number 201761) of additional clinical trials. In addition, the MAH took the opportunity to add a footnote in Table 3 in section 4.8 of the SmPC to align with Table 2 of the same section. Moreover, the RMP (version 14) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.23. Perampanel – FYCOMPA (CAP) - EMEA/H/C/002434/X/0025

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Julie Williams

Scope: Line extension to add a new strength of 0.5 mg/ml (EU/1/12/776/024) and add a new pharmaceutical form, oral solution
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.24. Pioglitazone – ACTOS (CAP) - EMEA/H/C/000285/WS/0848, GLUSTIN (CAP) - EMEA/H/C/000286/WS/0848; pioglitazone, glimepiride – TANDEMACT (CAP) - EMEA/H/C/000680/WS/0848; pioglitazone, metformin – COMPETACT (CAP) - EMEA/H/C/000655/WS/0848, GLUBRAVA (CAP) - EMEA/H/C/000893/WS/0848

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: Update of section 4.4 of the SmPC based on results of two long term observational cohort studies assessing bladder cancer risk with pioglitazone. The RMP is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.25. Ramucirumab – CYRAMZA (CAP) - EMEA/H/C/002829/II/0003

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with progression after platinum-based chemotherapy. As a consequence, sections 4.1, 4.2, 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

5.3.26. Trastuzumab emtansine – KADCYLA (CAP) - EMEA/H/C/002389/II/0019/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Grouped variation to amend Annex II of the product information to delete the obligation regarding the EMILIA (TDM4370g/BO21977) study (ANX 006). Furthermore, update of section 4.8 of the SmPC in order to update frequency of adverse drug reaction as a result of a pool data analysis from several clinical studies. The RMP is updated accordingly, including also changes related to inclusion and deletion of safety concerns in the RMP (enhanced pregnancy programme, evaluation of cardiac safety in patients with baseline left ventricular ejection fraction and efficacy of monotherapy versus trastuzumab associated to docetaxel). In addition, changes of final clinical study report (CSR) due dates for study KRISTINE (BO28408) and KAMILLA (mo28231) have been introduced. The MAH also took the opportunity to update the RMP following requests from previously assessed procedures (MEA 011.1 and ANX 007)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.27. Trastuzumab emtansine – KADCYLA (CAP) - EMEA/H/C/002389/II/0020/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Grouped variation to amend sections 4.2, 4.4 and 5.2 of the SmPC in order to update the safety information on hepatic impaired patients after analysis of study BO25499 in fulfilment of MEA 009. The Package Leaflet and the RMP are updated accordingly. The due date for the final study report for study BO25499 is also changed retrospectively
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: Extension of indication to include the treatment of patients with peripheral arterial disease (PAD). As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is also updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

6. Periodic safety update reports (PSURs)

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

6.1.1. Aclidinium bromide, formoterol – BRIMICA GENUAIR (CAP), DUAKLIR GENUAIR (CAP) - PSUSA/10307/201505

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

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

6.1.2. Apixaban – ELIQUIS (CAP) - PSUSA/00226/201505

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

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

6.1.3. Basiliximab – SIMULECT (CAP) - PSUSA/00301/201504

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

6.1.4. Cobicistat, darunavir – REZOLSTA (CAP) - PSUSA/10315/201505

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Amelia Cupelli

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

6.1.5. Dalbavancin – XYDALBA (CAP) - PSUSA/10350/201505

Applicant: Durata Therapeutics International B.V.

PRAC Rapporteur: Jolanta Gulbinovic

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

6.1.6. Decitabine – DACOGEN (CAP) - PSUSA/09118/201505

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Isabelle Robine

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

6.1.7. Efavirenz – STOCRIN (CAP), SUSTIVA (CAP) - PSUSA/01200/201504

Applicant: Merck Sharp & Dohme Limited; Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Margarida Guimarães

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

6.1.8. Epoetin theta – BIOPOIN (CAP), EPORATIO (CAP) - PSUSA/01240/201504

Applicant: Teva GmbH; Ratiopharm GmbH

PRAC Rapporteur: Isabelle Robine

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

6.1.9. Fidaxomicin – DIFICLIR (CAP) - PSUSA/01390/201505

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Qun-Ying Yue

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

6.1.10. Fluticasone furoate – AVAMYS (CAP) - PSUSA/09154/201504

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Adam Przybylkowski

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

6.1.11. Fluticasone furoate, vilanterol – RELVAR ELLIPTA (CAP), REVINTY ELLIPTA (CAP) - PSUSA/10099/201505

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Miguel-Angel Macia

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

6.1.12. Interferon beta-1a – AVONEX (CAP), REBIF (CAP) - PSUSA/09198/201505

Applicant: Biogen Idec; Merck Serono Europe Limited

PRAC Rapporteur: Dolores Montero Corominas

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

6.1.13. Ketoconazole – KETOCONAZOLE HRA (CAP) - PSUSA/10316/201505

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Viola Macolic Sarinic

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

6.1.14. Lidocaine, prilocaine – FORTACIN (CAP) - PSUSA/10110/201505

Applicant: Plethora Solutions Ltd.

PRAC Rapporteur: Miguel-Angel Macia

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

6.1.15. Linagliptin – TRAJENTA (CAP) - PSUSA/01886/201505

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

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

6.1.16. Linagliptin, metformin – JENTADUETO (CAP) - PSUSA/09214/201505

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

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

6.1.17. Misoprostol – HEMOPROSTOL (Art 58[2]) – EMEA/H/W/002652/PSUV/0004

Applicant: Linepharma International Limited

PRAC Rapporteur: Menno van der Elst

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

6.1.18. Nintedanib – VARGATEF (CAP) - PSUSA/10318/201505

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Leonidas Klironomos

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

6.1.19. Pixantrone dimaleate – PIXUVRI (CAP) - PSUSA/09261/201505

Applicant: CTI Life Sciences Limited

PRAC Rapporteur: Rafe Suvarna

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

6.1.20. Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) – PREPANDRIX (CAP)
Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP) - PSUSA/02281/201505

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Rafe Suvarna

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

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

6.1.21. Radium Ra^{223} dichloride – XOFIGO (CAP) - PSUSA/10132/201505

Applicant: Bayer Pharma AG
PRAC Rapporteur: Rafe Suvarna

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

6.1.22. Rilpivirine – EDURANT (CAP) - PSUSA/09282/201505

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Sabine Straus

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

6.1.23. Shingles (herpes zoster) vaccine (live) – ZOSTAVAX (CAP) - PSUSA/09289/201505

Applicant: Sanofi Pasteur MSD SNC

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

6.1.24. Simeprevir – OLYSIO (CAP) - PSUSA/10255/201505

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

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

6.1.25. Tafamidis – VYNDAQEL (CAP) - PSUSA/02842/201505

Applicant: Pfizer Limited

PRAC Rapporteur: Isabelle Robine

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

6.1.26. Tilmanocept – LYMPHOSEEK (CAP) - PSUSA/10313/201505

Applicant: Navidea Biopharmaceuticals Limited

PRAC Rapporteur: Jolanta Gulbinovic

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

6.1.27. Tolvaptan – SAMSCA (CAP) - PSUSA/02994/201505

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

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

6.1.28. Ulipristal – ELLAONE (CAP) - PSUSA/03074/201505

Applicant: Laboratoire HRA Pharma, SA

PRAC Rapporteur: Menno van der Elst

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

6.1.29. Vedolizumab – ENTYVIO (CAP) - PSUSA/10186/201505

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

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. Capecitabine – CAPECITABINE ACCORD (CAP), CAPECITABINE MEDAC (CAP), ECANSYA (CAP), XELODA (CAP), NAP - PSUSA/00531/201504

Applicant: Accord Healthcare Ltd; Medac Gesellschaft fuer klinische Spezialpraeparate m.b.H; Krka d.d. Novo mesto; Roche Registration Limited, various

PRAC Rapporteur: Martin Huber

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

6.2.2. Cytarabine – DEPOCYTE (CAP), NAP - PSUSA/00911/201503

Applicant: Pacira Ltd, various

PRAC Rapporteur: Rafe Suvarna

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

6.2.3. Methylthioninium chloride – METHYLTHIONINIUM CHLORIDE PROVEBLUE (CAP), NAP - PSUSA/02029/201505

Applicant: Provepharm SAS, various

PRAC Rapporteur: Qun-Ying Yue

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

6.2.4. Tacrolimus – ADVAGRAF (CAP), ENVARSUS (CAP), MODIGRAF (CAP), NAP - PSUSA/02839/201503

Applicant: Astellas Pharma Europe B.V.; Chiesi Farmaceutici S.p.A., various

PRAC Rapporteur: Almath Spooner

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. Acarbose (NAP) - PSUSA/00000017/201503

Applicant: various

PRAC Lead: Dolores Montero Corominas

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

6.3.2. Acetylsalicylic acid, bisoprolol (NAP) - PSUSA/00010287/201505

Applicant: various

PRAC Lead: Julie Williams

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

6.3.3. Amlodipine besilate, ramipril (NAP) - PSUSA/00000181/201503

Applicant: various

PRAC Rapporteur: Jan Neuhauser

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

6.3.4. Artemether, lumefantrin (dispersible tablet) (NAP) - PSUSA/00009060/201504

Applicant: various

PRAC Lead: Julie Williams

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

6.3.5. Captopril (NAP) - PSUSA/00000535/201504

Applicant: various

PRAC Lead: Julie Williams

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

6.3.6. Carmustine (powder and solvent for solution for infusion) (NAP) - PSUSA/00010349/201504

Applicant: various

PRAC Lead: Corinne Fechant

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

6.3.7. Ciprofloxacin hydrochloride, dexamethasone acetate (ear drops, suspension) (NAP) - PSUSA/00010012/201504

Applicant: various

PRAC Lead: Martin Huber

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

6.3.8. Dihydroergocristine (NAP) - PSUSA/00001071/201504

Applicant: various

PRAC Lead: Margarida Guimaraes

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

6.3.9. Dihydroergotamine (NAP) - PSUSA/00001075/201504

Applicant: various

PRAC Lead: Julie Williams

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

6.3.10. Dihydroergotoxine (NAP) - PSUSA/00001079/201504

Applicant: various

PRAC Lead: Jana Mlada

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

6.3.11. Human anti-D immunoglobulin (NAP) - PSUSA/00001614/201503

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

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

6.3.12. Influenza vaccine (split virion, inactivated) (NAP) - PSUSA/00010298/201504

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

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

6.3.13. Influenza vaccine (split virion, inactivated, prepared in cell cultures) (NAP) - PSUSA/00010299/201504

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 (surface antigen, inactivated) (NAP) - PSUSA/00001744/201504

Applicant: various

PRAC Lead: Carmela Macchiarulo

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

6.3.15. Influenza vaccine (surface antigen, inactivated, adjuvanted) (NAP) PSUSA/00010300/201504

Applicant: various

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, virosome) (NAP) - PSUSA/00001746/201504

Applicant: various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Metamizole (NAP) - PSUSA/00001997/201504

Applicant: various

PRAC Lead: Julia Pallos

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

6.3.18. Metformin (NAP) - PSUSA/00002001/201504

Applicant: various

PRAC Lead: Corinne Fechant

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

6.3.19. Nadroparin (NAP) - PSUSA/00002104/201503

Applicant: various

PRAC Lead: Dolores Montero Corominas

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

6.3.20. Nitrendipine (NAP) - PSUSA/00002171/201503

Applicant: various

PRAC Lead: Jan Neuhauser

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

6.3.21. Ofloxacin (systemic use) (NAP) - PSUSA/00002203/201504

Applicant: various

PRAC Lead: Torbjorn Callreus

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

6.3.22. Ofloxacin (topical use) (NAP) - PSUSA/00002204/201504

Applicant: various

PRAC Lead: Torbjorn Callreus

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

6.3.23. Paracetamol (intravenous formulation) (NAP) - PSUSA/00002311/201505

Applicant: various

PRAC Lead: Isabelle Robine

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

6.3.24. Promestriene (cream and vaginal capsules) (NAP) - PSUSA/00009271/201503

Applicant: various

PRAC Lead: Doris Stenver

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

6.3.25. Reboxetine (NAP) - PSUSA/00002615/201504

Applicant: various

PRAC Lead: Julie Williams

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

6.4. Follow-up to PSUR procedures

6.4.1. Iloprost – VENTAVIS (CAP) - EMEA/H/C/000474/LEG 037.1

Applicant: Bayer Pharma AG

PRAC Rapporteur: Isabelle Robine

Scope: MAH's responses to LEG 037 following PSUSA/00001724/201409 (special REVEAL registry study analysis) as adopted 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)[3]

7.1.1. Afamelanotide – SCENESSE (CAP) - EMEA/H/C/PSP/0033

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Draft protocol for a retrospective chart review study comparing long term safety data and outcome endpoints in patients receiving and not receiving Scenesse, or having discontinued the use of Scenesse. The second primary objective of the study should be the

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

assessment of the compliance with risk minimisation recommendations and the controlled access programme for patients receiving Scenesse
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[4]

7.2.1. Alglucosidase alfa – MYOZYME (CAP) - EMEA/H/C/000636/MEA/053.1

Applicant: Genzyme Europe BV

PRAC Rapporteur: Isabelle Robine

Scope: MAH's responses to MEA 053 [evaluation of a PASS protocol for epidemiology study ALGMYC07390: prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions] as adopted in June 2015
Action: For adoption of advice to CHMP

7.2.2. Dulaglutide – TRULICITY (CAP) - EMEA/H/C/002825/MEA/001.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: MAH's responses to MEA 001 [revised PASS protocol regarding the utilisation of dulaglutide in European countries: a cross-sectional, multi-country and multi-source drug utilisation study using electronic health record databases], as adopted in March 2015
Action: For adoption of advice to CHMP

7.2.3. Dulaglutide – TRULICITY (CAP) - EMEA/H/C/002825/MEA/002.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: MAH's responses to MEA 002 [revised PASS protocol on the utilisation and safety of dulaglutide in European countries: a modified prescription-event monitoring and network database study (multi-database collaborative research programme of observational studies)] request for supplementary information (RSI) as adopted in March 2015
Action: For adoption of advice to CHMP

7.2.4. Empagliflozin – JARDIANCE (CAP) - EMEA/H/C/002677/MEA/002.2

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Miguel-Angel Macia

Scope: MAH's responses to MEA 002.1 [PASS protocol for study 1245.96] request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

[4] 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

7.2.5. Empagliflozin – JARDIANCE (CAP) - EMEA/H/C/002677/MEA/004

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Miguel-Angel Macia

Scope: Draft protocol for a PASS (study 1245.97) to assess the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 diabetes: a multi-database European study
Action: For adoption of advice to CHMP

7.2.6. Flutemetamol (^{18}F) – VIZAMYL (CAP) - EMEA/H/C/002557/MEA/002.2

Applicant: GE Healthcare Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 002.1 [PASS protocol, study GE067-027 CPR to assess the effectiveness of the educational training programme] request for supplementary information (RSI) as adopted in July 2015
Action: For adoption of advice to CHMP

7.2.7. Panobinostat – FARYDAK (CAP) - EMEA/H/C/003725/MEA/002

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Draft protocol for a non-interventional PASS study (LBH589D2408) of panobinostat use in relapsed or relapsed/refractory multiple myeloma patients who have received at least two prior regimens including bortezomib and an immunomodulatory agent in a real-world setting according to the current EU prescribing information and document adherence to dosing regimen (including the dosing card, blister pack) by describing clinical characteristics, frequency and severity of the medication error events
Action: For adoption of advice to CHMP

7.2.8. Secukinumab – COSENTYX (CAP) - EMEA/H/C/003729/MEA/002.1

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's responses to MEA 002 [protocol for a non-interventional, non-imposed PASS to study the comparative safety of approved psoriasis therapies in a national cohort of psoriasis subjects treated by dermatologists/study No. Coronna-PSO-500] as adopted in June 2015
Action: For adoption of advice to CHMP

7.2.9. Tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/MEA/273

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Draft protocol for PASS study GS-EU-174-1846: a multicentre, non-interventional, retrospective cohort study of patients with chronic hepatitis B and with moderate or severe renal impairment treated with Viread
Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[5]

None

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

7.4.1. Agomelatine – THYMANAX (CAP) - EMEA/H/C/000916/II/0028; VALDOXAN (CAP) - EMEA/H/C/000915/II/0030 (without RMP)

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

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Submission of the final study report for PASS study CLE-20098- 068: an observational cohort study to evaluate the safety of agomelatine in standard medical practice in depressed patients. A prospective, observational (non-interventional), international, multicentre cohort study to fulfil a post-authorisation measure (MEA 006)
Action: For adoption of PRAC Assessment Report

7.4.2. Human normal immunoglobulin – FLEBOGAMMA DIF (CAP) - EMEA/H/C/000781/II/0043 (without RMP)

Applicant: Instituto Grifols S.A.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final clinisal study report (CSR) of the post-authorisation safety study (PASS): study IG1004 performed with Flebogamma DIF 50 mg/ml and 100 mg/ml to assess the tolerability of Flebogamma DIF 100 mg/ml in the clinical practice under routine conditions by comparing the frequency of infusions associated with potentially related adverse events between both strengths (to fulfil and additional pharmacovigilance activity, MEA 009.2)
Action: For adoption of PRAC Assessment Report

7.4.3. Retigabine – TROBALT (CAP) - EMEA/H/C/001245/II/0039 (with RMP)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

Scope: Submission of final results of study PRJ2250 entitled a 'survey of prescriber understanding of specific risks associated with Trobalt'. The RMP is revised to reflect the status and results of the study and associated conclusion on the effectiveness of current risk minimisation measures
Action: For adoption of PRAC Assessment Report

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

7.4.4. Saxagliptin – ONGLYZA (CAP) - EMEA/H/C/001039/WS/0839 Saxagliptin / metformin hydrochloride – KOMBOGLYZE (CAP) - EMEA/H/C/002059/WS/0839 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final clinical study report for an epidemiological study (PASS study category 3 not currently in the RMP) in order to compare the risk of hospitalisation for heart failure between dipeptidyl peptidase-4 inhibitors and sulfonylureas. In addition, a revised RMP (version 9) is submitted including other minor changes
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]

7.5.1. Alglucosidase alfa – MYOZYME (CAP) - EMEA/H/C/000636/MEA/056

Applicant: Genzyme Europe BV

PRAC Rapporteur: Isabelle Robine

Scope: Interim report from a healthcare pofessional survey that measure the effectiveness of the approved safety information packet (SIP)
Action: For adoption of advice to CHMP

7.5.2. Darunavir – PREZISTA (CAP) - EMEA/H/C/000707/MEA/069.3

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Interim results from PENTA study: an observational study to assess growth abnormalities (height) in human immunodeficiency virus (HIV)-infected children and adolescents on antiretroviral therapy in Europe, with special reference to darunavir (category 3)
Action: For adoption of advice to CHMP

7.5.3. Etravirine – INTELENCE (CAP) - EMEA/H/C/000900/MEA/049.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Isabelle Robine

Scope: Submission of second annual report on study TMC125-EPPICC: a pharmacovigilance study to define the long-term safety profile of etravirine in human inmmunodeficiency virus (HIV)-1-infected children and adolescents in Europe
Action: For adoption of advice to CHMP

7.5.4. Fampridine – FAMPYRA (CAP) - EMEA/H/C/002097/MEA/017

Applicant: Biogen Idec Ltd.

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

PRAC Rapporteur: Sabine Straus

Scope: Annual progress report of an observational safety study (protocol no: 218MS401) to collect information on safety and to document the drug utilisation of Fampyra when used in routine medical practice (LIBERATE)
Action: For adoption of advice to CHMP

7.5.5. Indacaterol, glycopyrronium bromide – ULTIBRO BREEZHALER (CAP) - EMEA/H/C/2679/MEA 003.3; ULUNAR BREEZHALER (CAP) - EMEA/H/C/3875/MEA 004.2; XOTERNA BREEZHALER (CAP) - EMEA/H/C/3755/MEA 003.3;

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: MAH's response to MEA 003.2 [Drug utilisation study – First interim report CQVA 149A2401] request for supplementary information (RSI) as adopted in October 2015
Action: For adoption of advice to CHMP

7.5.6. Infliximab – INFLECTRA (CAP) - EMEA/H/C/002778/MEA/008.1; REMSIMA (CAP) - EMEA/H/C/002576/MEA/008.1

Applicant: Hospira UK Limited, Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Rafe Suvarna

Scope: Fifth periodic report for post marketing surveillance of Remsima 100 mg to evaluate safety and efficacy in Korea
Action: For adoption of advice to CHMP

7.5.7. Ivacaftor – KALYDECO (CAP) - EMEA/H/C/002494/MEA/023

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Miguel-Angel Macia

Scope: Submission of annual interim analysis data for study VX12-770-115 : an ocular safety study of ivacaftor-treated pediatric patients 11 years of age or younger with cystic fibrosis. report L113, version 1.0.
Action: For adoption of advice to CHMP

7.5.8. Ketoconazole – KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/MEA/004.1

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Viola Macolic Sarinic

Scope: Final report from named patient basis programme in France (ATU de cohorte): to further characterize the risk of hepatotoxicity in terms of frequency, symptoms in a real life use, potential risk factors, and consequences
Action: For adoption of advice to CHMP

7.5.9. Mannitol – BRONCHITOL (CAP) - EMEA/H/C/001252/ANX/002.7

Applicant: Pharmaxis Pharmaceuticals Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 002.6 (4th interim interim analysis of the cystic fibrosis (CF) study) as adopted in July 2015
Action: For adoption of advice to CHMP

7.5.10. Micafungin – MYCAMINE (CAP) - EMEA/H/C/000734/MEA/013.1

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Annual interim report from an observational database-assisted comparative cohort study to investigate the risk of hepatotoxicity and hepatocellular carcinoma (protocol number: ISN 9463-CL-140): a multicentre cohort study of the short and long-term safety of micafungin and Other parenteral antifungal agents (MYCOS)
Action: For adoption of advice to CHMP

7.5.11. Ustekinumab – STELARA (CAP) - EMEA/H/C/000958/MEA/023.7

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 023.6 [Fifth interval safety registry report (protocol: CNTO1275PSO4005) Nordic Database] request for supplementary information (RSI) as adopted in July 2015
Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Elvitegravir – VITEKTA (CAP) - EMEA/H/C/002577/MEA/007.2

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: MAH's responses to MEA 007.1 [Feasibility study / drug utilisation study (DUS) GS-EU-183-1335] request for supplementary information (RSI) as adopted in June 2015
Action: For adoption of advice to CHMP

7.6.2. Gadoversetamide – OPTIMARK (CAP) - EMEA/H/C/000745/ANX/014.6

Applicant: Mallinckrodt Deutschland GmbH

PRAC Rapporteur: Rafe Suvarna

Scope: From R/012: Responses to request for supplementary information / response to outcome of teleconference from 27 July 2015 to evaluate options for protocol amendments of study no. ALS-Gd64/001
Action: For adoption of advice to CHMP

See also under 11.2.1. Gadolinium-containing contrast agents (GdCAs)

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.

None

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.

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Alipogene tiparvovec – GLYBERA (CAP) - EMEA/H/C/002145/S/0051 (without RMP)

Applicant: uniQure biopharma B.V.

PRAC Rapporteur: Julie Williams

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

8.1.2. Cholic acid – ORPHACOL (CAP) - EMEA/H/C/001250/S/0012 (without RMP)

Applicant: Laboratoires CTRS - Boulogne Billancourt

PRAC Rapporteur: Rafe Suvarna

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

8.1.3. Tocofersolan – VEDROP (CAP) - EMEA/H/C/000920/S/0015 (without RMP)

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

PRAC Rapporteur: Julie Williams

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

8.2. Conditional renewals of the marketing authorisation

None

8.3. Renewals of the marketing authorisation

8.3.1. Belatacept – NULOJIX (CAP) - EMEA/H/C/002098/R/0031 (with RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

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

8.3.2. Belimumab – BENLYSTA (CAP) - EMEA/H/C/002015/R/0036 (with RMP)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

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

8.3.3. Boceprevir – VICTRELIS (CAP) - EMEA/H/C/002332/R/0036 (with RMP)

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Isabelle Robine

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

8.3.4. Exenatide – BYDUREON (CAP) - EMEA/H/C/002020/R/0031 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

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

8.3.5. Natalizumab – TYSABRI (CAP) - EMEA/H/C/000603/R/0091 (with RMP)

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

8.3.6. Rivastigmine – RIVASTIGMINE ACTAVIS (CAP) - EMEA/H/C/002036/R/0016 (without RMP)

Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Isabelle Robine

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

8.3.7. Tobramycin – TOBI PODHALER (CAP) - EMEA/H/C/002155/R/0034 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Sabine Straus

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

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

9.2. 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

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. Mitoxantrone (NAP) – EMA/H/A-30/1399

Applicant: Meda Pharma GmbH and associated companies (Novantrone)

PRAC Lead: Sabine Straus

Scope: PRAC consultation on the need for additional risk minimisation measures regarding the risk of leukaemia and cardiotoxicity as part of an ongoing referral procedure under Article 30 of Directive 2001/83/EC
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. Androstanolone (NAP)

Applicant: Besins Healthcare (Andractim), various

PRAC Rapporteur: Corinne Fechant

Scope: PRAC consultation on the applicability of the PRAC recommendation of the 2014 referral procedure on testosterone and cardiovascular safety under Article 31 of Directive 2001/83/EC to androstanolone
Action: For adoption of advice to CHMP

11.2. Other requests

11.2.1. Gadolinium-containing contrast agents (GdCA): Gadobenate dimeglumine; gadobutrol; gadodiamide; gadopentetic acid dimeglumine, gadoteric acid (intra-articular formulation); gadoteric acid (intravenous and intravascular formulations); gadoteridol; gadoxetic acid disodium (NAP)

Applicant: various

Lead member: Rafe Suvarna

Scope: PRAC consultation on a post-authorisation measure to conduct further clinical studies to assess the retention of gadolinium in bone resulting from the 2010 referral procedures under Article 20 of Regulation (EC) 726/2004 and Article 31 of Directive 2001/83/EC for gadolinium-containing contrast agents
Action: For adoption of advice to Member States

See also under 7.6.2. Gadoversetamide

11.2.2. Tramadol, paracetamol (NAP) - PT/H/0919/002/E01

Applicant: PTR Pharma Consulting, Lda (Tramadol Paracetamol Litexil)

Lead member: Margarida Guimarães

Scope: PRAC consultation on a CMDh procedure evaluated under Article 29(1) of Directive 2001/83/EC following a disagreement between Member States on the risk management plan and the need for a drug utilisation study (DUS)
Action: For adoption of advice to Member States/CMDh

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 pharmacovigilance - organ maturation tables

Action: For discussion

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

12.3.1. Scientific Advice Working Party (SAWP) – consultation procedure: involving the PRAC outside the pilot for non-imposed PASS protocols

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. EMA Management Board data gathering initiative

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

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. Periodic safety update

None

12.10.3. Project and Maintenance Group (PMG) 2 - roadmap for PSUR issues: preparation for workshop in January 2016

PRAC lead: Margarida Guimaraes, Menno van der Elst
Action: For discussion

12.10.4. PSURs repository

None

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

Action: For adoption of the revised list

12.11. Signal management

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

PRAC lead: Sabine Straus
Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Additional monitoring

None

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

Action: For adoption

12.12.3. Management and reporting of adverse reactions to medicinal products – guidance on monitoring of off label use

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality - EudraVigilance auditable requirement technical implementation

Action: For discussion

12.13.2. Activities related to the confirmation of full functionality – EudraVigilance audit tender

Action: For adoption

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

13. Any other business

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

Action: For adoption

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

Action: For discussion

13.3. Strategy on impact of pharmacovigilance

Action: For adoption

13.4. Update on Pharmacovigilance systems and services

Action: For discussion

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/