26 September 2016
EMA/PRAC/635914/2016
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 26-29 September 2016

Chair: June Raine – Vice-Chair: Almath Spooner

26 September 2016, 13:00 – 19:30, room 3/A

27 September 2016, 08:30 – 19:30, room 3/A

28 September 2016, 08:30 – 19:30, room 3/A

29 September 2016, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

13 October 2016, 9:00 – 12:00, room 7/B, via teleconference

Health and safety information

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

Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure 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

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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 October 2016 plenary session to be held 26-29 September 2016. See October 2016 PRAC minutes (to be published post November 2016 PRAC meeting).

1.2. Adoption of agenda of the meeting of 26-29 September 2016

None

1.3. Adoption of the minutes of the previous meeting of 30 August–2 September 2016

None

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. Gadolinium-containing contrast agents (GdCA): gadobenic acid (NAP); gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP); gadoversetamide – OPTIMARK (CAP) - EMEA/H/A-31/1437

Applicant: Mallinckrodt Deutschland GmbH (Optimark); various

PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Doris Stenver

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

Action: For adoption of a list of outstanding issues (LoOI) (or recommendation to CHMP)

3.2.2. Retinoids: acitretin (NAP); adapalene (NAP); alitretinoin - PANRETIN (CAP); bexarotene – TARGRETIN (CAP); isotretinoin (NAP); tazarotene (NAP); tretinoin (NAP) - EMEA/H/A-31/1446

Applicant: Eisai Ltd (Panretin, Targretin), various

PRAC Rapporteur: Leonor Chambel; PRAC Co-rapporteur: Julie Williams

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

Action: For discussion on the need for a public hearing

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. Lenvatinib – LENVIMA (CAP)

Applicant: Eisai Europe Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of cholecystitis

Action: For adoption of PRAC recommendation

EPITT 18750 – New signal

Lead Member State: SE

4.1.2. Nivolumab – OPDIVO (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of pemphigoid

Action: For adoption of PRAC recommendation

EPITT 18759 – New signal

Lead Member State: DE

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Adalimumab – HUMIRA (CAP) - EMEA/H/C/000481/SDA/092

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of acute febrile neutrophilic dermatosis (Sweet's syndrome)

Action: For adoption of PRAC recommendation

EPITT 18630 – Follow-up to April 2016

[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

4.3.2. Anakinra - KINERET (CAP) - EMEA/H/C/000363/SDA/027; canakinumab - ILARIS (CAP) - EMEA/H/C/001109/SDA/047

Applicant: Swedish Orphan Biovitrum AB (publ) (Kineret), Novartis Europharm Ltd (Ilaris)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of weight increase

Action: For adoption of PRAC recommendation

EPITT 18641 – Follow-up to May 2016

4.3.3. Dexlansoprazole (NAP); lansoprazole (NAP)

Applicant: various

PRAC Rapporteur: Kirsti Villikka

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

Action: For adoption of PRAC recommendation

EPITT 18645 – Follow-up to May 2016

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

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

PRAC Rapporteur: Valerie Strassmann

Scope: Signal of aortic aneurysm and dissection

Action: For adoption of PRAC recommendation

EPITT 18651 – Follow-up to May 2016

4.3.5. Levetiracetam (oral solution) – KEPPRA (CAP) – EMEA/H/C/000277/SDA/082, NAP

Applicant: UCB Pharma SA, various

PRAC Rapporteur: Veerle Verlinden

Scope: Signal of medication errors associated with accidental overdose

Action: For adoption of PRAC recommendation

EPITT 10519 – Follow-up to May 2016

4.3.6. Metronidazole (NAP)

Applicant: various

PRAC Rapporteur: Martin Huber

Scope: Signal of severe hepatic and neurologic toxicity in patients with Cockayne syndrome

Action: For adoption of PRAC recommendation

EPITT 18663 – Follow-up to May 2016

4.3.7. Paracetamol (NAP)

Applicant: various

PRAC Rapporteur: Veerle Verlinden

Scope: Signal of paracetamol use in pregnancy and child neurodevelopment

Action: For adoption of PRAC recommendation

EPITT 17796 – Follow-up to May 2014

4.3.8. Propofol (NAP)

Applicant: various

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Signal of diabetes insipidus

Action: For adoption of PRAC recommendation

EPITT 18622 – Follow-up to March 2016

4.3.9. Regorafenib - STIVARGA (CAP) - EMEA/H/C/002573/SDA/008

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

Scope: Signal of angioedema

Action: For adoption of PRAC recommendation

EPITT 18656 – Follow-up to May 2016

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Baricitinib - EMEA/H/C/004085

Scope: Treatment of moderate to severe active rheumatoid arthritis (RA)

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

5.1.2. Insulin glargine, lixisenatide - EMEA/H/C/004243

Scope: Treatment of adults with type 2 diabetes mellitus

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

5.1.3. Prasterone - EMEA/H/C/004138

Scope: Treatment of vulvovaginal atrophy

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

5.1.4. Rituximab - EMEA/H/C/004112

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

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

5.1.5. Trientine tetrahydrochloride - EMEA/H/C/004005, Orphan

Applicant: GMP-Orphan SA

Scope: Treatment of Wilson's disease

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. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/II/0019

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Updated RMP in order to include information regarding additional risk minimisation measures (i.e. healthcare professionals' material highlighting the existence of the registry) as outlined in Annex II. In addition, the MAH took the opportunity to introduce administrative changes to the protocol of the registry study, to add information about the renal pharmacokinetics study, updated information about off-label use during post-marketing experience and to include further administrative changes to the RMP

Action: For adoption of PRAC Assessment Report

5.2.2. Duloxetine - ARICLAIM (CAP) - EMEA/H/C/000552/WS1015/0065; CYMBALTA (CAP) - EMEA/H/C/000572/WS1015/0069; DULOXETINE LILLY (CAP) - EMEA/H/C/004000/WS1015/0005; XERISTAR (CAP) -

EMEA/H/C/000573/WS1015/0072; YENTREVE (CAP) - EMEA/H/C/000545/WS1015/0055

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Updated RMP to add a new observational study to assess maternal and foetal outcomes following exposure to duloxetine (F1J-MC-B057) and to update the plans for the existing pregnancy registry (F1JMC-B034)

Action: For adoption of PRAC Assessment Report

5.2.3. Epoetin alfa - ABSEAMED (CAP) - EMEA/H/C/000727/WS1011/0057; BINOCRIT (CAP) - EMEA/H/C/000725/WS1011/0058; EPOETIN ALFA HEXAL (CAP) - EMEA/H/C/000726/WS1011/0056

Applicant: SANDOZ GmbH

PRAC Rapporteur: Claire Ferard

Scope: Updated RMP as per the outcome of the PSUR single assessment procedure (EMEA/H/C/PSUSA/00001237/201508) dated April 2016 in order to change the risk classification for 'hyperkalemia' and 'hypersensitivity reactions (including anaphylactic reactions)' from important potential risks to important identified risks and to review the table of safety concerns accordingly. Furthermore, the MAH took the opportunity to update the RMP to include changes following the variation approval to add the subcutaneous route of administration in nephrology indications (EMEA/H/C/725-727/WS/0877) dated March 2016. In addition, minor RMP changes were introduced

Action: For adoption of PRAC Assessment Report

5.2.4. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/II/0199

Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Updated RMP (version 6.0) in order to remove 'injection site reactions' as an important potential risk and 'use in pregnant women', 'use in hepatic and renal impaired subjects' and 'use in different ethnic origins' as missing information. In addition, the MAH took the opportunity to amend the due dates of several category 3 studies, to align the RMP with GVP module V on risk management systems (revision 1), to review the list of studies included in the pharmacovigilance plan and to update the clinical trials and post-marketing experience

Action: For adoption of PRAC Assessment Report

5.2.5. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/II/0103

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Eva Segovia

Scope: Updated RMP (version 9.0) in order to add hepatitis B reactivation as a new

important identified risk

Action: For adoption of PRAC Assessment Report

5.2.6. Nilotinib - TASIGNA (CAP) - EMEA/H/C/000798/II/0083

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Updated RMP (version 15) in order to add hepatitis B reactivation as a new important identified risk

Action: For adoption of PRAC Assessment Report

5.2.7. Posaconazole - NOXAFIL (CAP) - EMEA/H/C/000610/II/0040

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Updated RMP (version 12.0) in order to reflect the study results showing a lack of interaction effect of OATP1B1 and OATP1B3 substrates and inhibitors

Action: For adoption of PRAC Assessment Report

5.2.8. Roflumilast – DALIRESP (CAP) - EMEA/H/C/002398/WS1037; DAXAS (CAP) - EMEA/H/C/001179/WS1037; LIBERTEK (CAP) - EMEA/H/C/002399/WS1037

Applicant: Takeda GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Updated RMP (version 17.0) in order to reflect the modified availability date, from 'Q3 2016' to 'Q2 2017', for the results of study RO-2455-302-RD (FUM 004) entitled 'A multicentre, randomized, double-blind phase 3 study to evaluate tolerability and pharmacokinetics of 500µg roflumilast once daily with an up-titration regimen in Chronic obstructive pulmonary disease (COPD), including an open-label down-titration period evaluating tolerability and pharmacokinetics of 250µg roflumilast once daily in subjects not tolerating 500µg roflumilast once-daily'

Action: For adoption of PRAC Assessment Report

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

5.3.1. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/II/0058

Applicant: Teva B.V.

PRAC Rapporteur: Claire Ferard

Scope: Extension of indication to include the induction of remission, and the consolidation in adult patients with newly diagnosed low-to-intermediate risk acute promyelocytic leukaemia (APL) (white blood cell count, ≤ 10 x 10^3/µl) characterised by the presence of

the t(15;17) translocation and/or the presence of the pro-myelocytic leukaemia/retinoic-acid-receptor-alpha (PML/RAR-alpha) gene for Trisenox. As a consequence, sections 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated regarding the posology, efficacy and safety information and warnings. In addition, a RMP is introduced. The Package Leaflet is updated accordingly

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

5.3.2. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0054

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final clinical study report (CSR) for study AS001, a phase 3, multicentre, randomized, double-blind, placebo-controlled study to evaluate efficacy and safety of certolizumab pegol in subjects with active axial spondyloarthritis (axSpA). As a consequence, sections 4.8 and 5.1 of the SmPC are revised in order to update the efficacy and safety information (week 204) for study AS001. The RMP (version 11.0) is updated accordingly. The package leaflet remains unchanged

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

5.3.3. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0055

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final clinical study report (CSR) for study PsA001, a phase 3, multicentre, randomized, double-blind, parallel group, placebo-controlled study to evaluate the efficacy and safety of certolizumab pegol in subjects with adult onset active and progressive psoriatic arthritis (PsA), in order to provide data on long-term use of Cimzia in psoriatic arthritis subjects up to 216 weeks of treatment. As a consequence, sections 4.8 and 5.1 of the SmPC are revised in order to update the efficacy and safety information (week 216) for study PsA001. The RMP (version 11) is updated accordingly. The package leaflet remains unchanged

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

5.3.4. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/X/0055/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Line extension to introduce a new pharmaceutical form associated with new strengths (1 mg, 2.5 mg and 5 mg hard capsules) grouped with a type II variation to include paediatric use in the approved indication. As a consequence, sections 4.2 and 4.4 of the SmPC are updated to detail the posology in paediatric patients and to update the safety information respectively. The Package Leaflet and Labelling are updated

accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the product information is brought in line with the latest QRD template (version 10)

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

5.3.5. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0057

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.6 of the SmPC in order to delete references to the pregnancy and lactation surveillance programmes. The Package Leaflet and the RMP are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial updates to the product information

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

5.3.6. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0045

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of hypercalcemia of malignancy refractory to intravenous bisphosphonate. As a consequence, sections 4.2, 4.3, 4.8, 5.1 and 5.3 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

5.3.7. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0046

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.6 of the SmPC in order to delete references to the pregnancy and lactation surveillance programmes. The Package Leaflet and the RMP are updated accordingly. In addition, the MAH took the opportunity to make minor editorial updates to the product information

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

5.3.8. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0012

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety

information to reflect findings from a recently completed phase 3b study (study H9X-MC-GBDG (GBDG)) concerning the use of dulaglutide in combination with sulphonylurea alone. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)

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

5.3.9. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0013

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.2, 4.7, 4.8 and 5.1 of the SmPC for Trulicity following completion of a phase 3b study (study H9X-MCGBDI (GBDI)) to reflect the study's findings concerning the use of dulaglutide in combination with basal insulin. The Package Leaflet 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/0032

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Eva Segovia

Scope: Update of the SmPC section 4.4 and 4.8 to include new information on drug-induced liver injury. As a consequence, Annex II relating to 'key elements to be included in the educational material' is revised. The RMP (version 39) is updated accordingly

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

5.3.11. Eltrombopag - REVOLADE (CAP) - EMEA/H/C/001110/II/0035/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Eva Segovia

Scope: Submission of the clinical study report (CSR) for study TRC112765 exploring the safety of eltrombopag in subjects with solid tumours receiving gemcitabine monotherapy or gemcitabine plus cisplatin or carboplatin. The RMP (version 40) is updated accordingly. In addition, the MAH took the opportunity to revise due dates for submission of final reports for two studies in the pharmacovigilance plan

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

5.3.12. Eltrombopag - REVOLADE (CAP) - EMEA/H/C/001110/II/0036/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations to update Annex II of the product information based on the study assessing the 'effectiveness of the eltrombopag educational materials for hepatitis C associated thrombocytopenia'. The RMP (version 41) is updated by removing the PASS study PLATELET (post-authorisation safety study with eltrombopag: multicentre, prospective, observational cohort study of thromocytopenic hepatitis C virus (HCV) patients receiving eltrombopag) and submission of the final report for ENABLE-TEE study WWE116951/CET115A2404: a prospective observational study to understand later outcome patterns among patients with and without a thromboembolic event

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

5.3.13. Eslicarbazepine acetate - ZEBINIX (CAP) - EMEA/H/C/000988/X/0050/G

Applicant: Bial - Portela & Cª, S.A.

PRAC Rapporteur: Martin Huber

Scope: Grouping of a line extension application to add a new pharmaceutical form (50 mg/ml oral suspension) and a type II variation (new indication) to add the treatment of children aged 2 years and older. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC, the Package Leaflet and the RMP (version 14.0) are updated accordingly

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

5.3.14. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/II/0040

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Update of section 4.6 of the SmPC to add information on the use of fingolimod in pregnancy. In addition, section 5.3 of the SmPC is updated to include information about dose correspondence between human and animal species used for the preclinical tests of teratogenicity. The RMP (version 12.0) is updated accordingly. The MAH took the opportunity to introduce minor editorial changes in sections 4.4, 4.5, 4.6 and 5.2 of the SmPC and in Annex II

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

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

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Grouped variations to update sections 4.4, 4.8 and 5.1 of the SmPC in order to

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

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

5.3.16. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0067

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information with the data from the final clinical study reports of studies C0524T18 and P07642 in fulfilment of MEA 031 and MEA 032. In addition, the MAH took the opportunity to combine the SmPC for the pre-filled pen and pre-filled syringe for 50 mg strength and for the pre-filled pen and pre-filled syringe for 100 mg strength respectively, in line with the latest QRD template (version 9.1). The RMP (version 15) is updated accordingly

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

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

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Line extension to introduce a new pharmaceutical form (20mg/ml oral solution) and two new strengths of film-coated tablets (25mg and 75mg) to the currently approved presentations for Celsentri, grouped with an extension of indication to include paediatric use (2 to 18 years). As a consequence, sections 4.2 and 4.4 of the SmPC are updated to detail posology in paediatric patients and to update the safety information respectively. The Package Leaflet and Labelling are updated accordingly. Furthermore, the product information is brought in line with the latest QRD template (version 10)

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

5.3.18. Nilotinib - TASIGNA (CAP) - EMEA/H/C/000798/II/0084/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations to 1) update of the 150 mg SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1 and Package Leaflet based on the results from study CAMN107I2201 (ENESTFreedom): a Phase II, single-arm study evaluating nilotinib treatment

discontinuation (treatment-free remission (TFR)) in newly-diagnosed patients with Philadelphia chromosome-positive chronic myelogenous leukaemia in chronic phase (Ph+ CML-CP) who achieved a sustained deep molecular response; 2) Update of the 150 mg and 200 mg SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1 and Package Leaflet based on the results from study CAMN107A2408 (ENESTop): a Phase II, single-arm study evaluating nilotinib treatment discontinuation (treatment-free remission (TFR)) in patients with Ph+ CML-CP who achieved a sustained deep molecular response on nilotinib treatment after switching from imatinib treatment; 3) Update of the 200 mg SmPC sections 4.8 and 5.1, based on the results from study CAMN107A2405 (ENESTcmr): a Phase III open-label, randomised study to evaluate nilotinib or imatinib treatment in patients with Ph+ CML-CP who have not achieved a deep molecular response after previous imatinib therapy. The RMP (version 16) is updated accordingly. Furthermore, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)

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

5.3.19. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0012

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the monotherapy treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL): - after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin, or - after at least two prior therapies in patients who are not candidates for ASCT. As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the proposed new indication, add a warning that patients with active autoimmune disease and symptomatic interstitial lung disease were excluded from clinical trials of cHL, and update the safety and pharmacodynamic information. The Package Leaflet and the RMP (version 5.0) are updated accordingly. Furthermore, the product information is brought in line with the latest QRD template (version 10.0)

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

5.3.20. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0017

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of recurrent or metastatic squamous cell cancer of the head and neck (SCCHN) after platinum-based therapy in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, of the SmPC are updated in order to add the proposed new indication, add a warning that patients with a baseline performance score ≥ 2, untreated brain metastasis, active autoimmune disease, or medical conditions requiring systemic immunosuppression were excluded from the SCCHN clinical trial and update the undesirable effects and safety information. The Labelling and RMP (version 6.0) are updated accordingly

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

CHMP

5.3.21. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0018

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the safety information for toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), myositis, myocarditis and rhabdomyolysis based on findings from routine pharmacovigilance activities. The Package Leaflet and RMP (version 4.5) are updated accordingly

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

5.3.22. Ocriplasmin - JETREA (CAP) - EMEA/H/C/002381/II/0026

Applicant: ThromboGenics NV

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC to reflect new long-term safety and efficacy data based on the final clinical study report for study TG-MV-014 in fulfilment of MEA 002. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the annexes, to align the annexes with the latest QRD templates (versions 9.1 and 10). The RMP (version 7) is updated accordingly

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

5.3.23. Pazopanib - VOTRIENT (CAP) - EMEA/H/C/001141/II/0038

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Update of section 4.6 of the SmPC to add male contraception following a review of pazopanib according to the MAH's guideline on prevention of pregnancies. The Package Leaflet and the RMP (version 16) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10) and combine the SmPC of the two tablets strengths

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

5.3.24. Raltegravir - ISENTRESS (CAP) - EMEA/H/C/000860/X/0059

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Line extension to add a new strength of 600mg film coated tablets

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

5.3.25. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0061

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of visual impairment due to choroidal neovascularization (CNV) based on 6-month data from the pivotal study CRFB002G2301 (MINERVA). As a consequence, SmPC sections 4.1, 4.2, 4.8 and 5.1 are updated. The Package Leaflet and the RMP (version 16.0) are updated accordingly

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

5.3.26. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0031

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information for myelofibrosis following the completion of two 5-year follow up studies: INCB 18424-351 (randomized, double-blind, placebo-controlled study of the ruxolitinib tablets administered orally to subjects with primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis) and INC424A2352 (randomized study of ruxolitinib tablets compared to best available therapy in subjects with primary myelofibrosis, post-polycythemia vera-myelofibrosis or post-essential thrombocythemia myelofibrosis). Annex II 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/0005

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.8 and 5.1 of the SmPC and Annex II to implement the results from the pivotal study CLDE225A2201 (phase II, randomized double-blind study of efficacy and safety of two dose levels of LDE225 in patients with locally advanced or metastatic basal cell carcinoma) and related analyses (correlative analysis of Gli1 data and molecular analysis in tumour material). The RMP (version 4.0) is updated accordingly

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

5.3.28. Temsirolimus - TORISEL (CAP) - EMEA/H/C/000799/II/0063

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Final results from study 3066K1-4438-WW (B1771007) entitled 'a randomized phase 4 study comparing two intravenous temsirolimus (TEMSR) regimens in subjects with relapsed, refractory mantle cell lymphoma' and fulfilment of obligation to conduct post authorisation measure ANX 027.2. In addition, submission of the toxic effects of interest (e.g. bleeding, infection- and mucositis-related events0 for study 3066K1-4438-WW (post-marketing commitment MEA 028) together with a review discussing potential new safety concerns arising from the results. The RMP (version3.0) is updated accordingly to add myocardial infarction and cardiovascular events in patient with coexisting cardiovascular conditions as important potential risks, and anaemia, thrombocytopenia, hypercholesterolemia, and hypertriglyceridemia as important identified risks. Furthermore, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

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

5.3.29. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/II/0016

Applicant: AstraZeneca AB

PRAC Rapporteur: Claire Ferard

Scope: Extension of indication to include the treatment of paediatric population. As a consequence, sections 4.1, 4.2, 4.6, 4.8, 5.1 and 5.2 of the SmPC are amended. The Package Leaflet is 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. Albiglutide - EPERZAN (CAP) - PSUSA/00010175/201603

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alirocumab - PRALUENT (CAP) - PSUSA/00010423/201603

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Apremilast - OTEZLA (CAP) - PSUSA/00010338/201603

Applicant: Celgene Europe Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Bedaquiline - SIRTURO (CAP) - PSUSA/00010074/201603

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Belimumab - BENLYSTA (CAP) - PSUSA/00009075/201603

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Betaine anhydrous[2] - CYSTADANE (CAP) - PSUSA/00000390/201602

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

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Bosutinib - BOSULIF (CAP) - PSUSA/00010073/201603

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

[2] Centrally authorised product only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Cabozantinib - COMETRIQ (CAP) - PSUSA/00010180/201603

Applicant: TMC Pharma Services Ltd

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Cangrelor - KENGREXAL (CAP) - PSUSA/00010360/201603

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Ceftolozane, tazobactam - ZERBAXA (CAP) - PSUSA/00010411/201603

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Cholic acid[3] - KOLBAM (CAP) - PSUSA/00010182/201603

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Cholic acid[4] - ORPHACOL (CAP) - PSUSA/00010208/201603

Applicant: Laboratoires CTRS - Boulogne Billancourt

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[3] Treatment of inborn errors in primary bile acid synthesis: cerebrotendinous xanthomatosis (CTX) deficiency, 2- (or α-) methylacyl-CoA racemase (AMACR) deficiency or cholesterol 7α-hydroxylase (CYP7A1) deficiency indications
[4] Treatment of inborn errors in primary bile acid synthesis: oxosteroid-reductase or hydroxy-steroid dehydrogenase deficiency indications

6.1.13. Ciclosporin[5] - IKERVIS (CAP) - PSUSA/00010362/201603

Applicant: Santen Oy

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Cinacalcet - MIMPARA (CAP) - PSUSA/00000756/201602

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Collagenase clostridium histolyticum[6] - XIAPEX (CAP) - PSUSA/00000871/201602

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Dabigatran - PRADAXA (CAP) - PSUSA/00000918/201603

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Dexmedetomidine - DEXDOR (CAP) - PSUSA/00000998/201603

Applicant: Orion Corporation

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dulaglutide - TRULICITY (CAP) - PSUSA/00010311/201603

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

[5] Topical use only
[6] Treatment of Dupuytren's contracture and treatment of Peyronie's disease

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Enfuvirtide - FUZEON (CAP) - PSUSA/00001217/201603

Applicant: Roche Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Ferric citrate coordination complex - FEXERIC (CAP) - PSUSA/00010418/201603

Applicant: Keryx Biopharma UK Ltd.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Fingolimod - GILENYA (CAP) - PSUSA/00001393/201602

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Guanfacine - INTUNIV (CAP) - PSUSA/00010413/201603

Applicant: Shire Pharmaceuticals Ireland Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Influenza vaccine (split virion, inactivated)[7] - IDFLU (CAP); INTANZA (CAP) - PSUSA/00001743/201603

Applicant: Sanofi Pasteur MSD SNC

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[7] Centrally authorised products only

6.1.24. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - OPTAFLU (CAP) - PSUSA/00001745/201603

Applicant: Novartis Influenza Vaccines Marburg GmbH

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Isavuconazole - CRESEMBA (CAP) - PSUSA/00010426/201603

Applicant: Basilea Medical Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Lapatinib - TYVERB (CAP) - PSUSA/00001829/201603

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Mepolizumab - NUCALA (CAP) - PSUSA/00010456/201603

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Mifamurtide - MEPACT (CAP) - PSUSA/00002059/201603

Applicant: Takeda France SAS

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Naloxegol - MOVENTIG (CAP) - PSUSA/00010317/201603

Applicant: AstraZeneca AB

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Oritavancin - ORBACTIV (CAP) - PSUSA/00010368/201603

Applicant: The Medicines Company UK Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Ospemifene - SENSHIO (CAP) - PSUSA/00010340/201602

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Pembrolizumab - KEYTRUDA (CAP) - PSUSA/00010403/201603

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Pirfenidone - ESBRIET (CAP) - PSUSA/00002435/201602

Applicant: Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.35. Riociguat - ADEMPAS (CAP) - PSUSA/00010174/201603

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Sebelipase alpha - KANUMA (CAP) - PSUSA/00010422/201602

Applicant: Alexion Europe SAS

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Tedizolid phosphate - SIVEXTRO (CAP) - PSUSA/00010369/201603

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Teduglutide - REVESTIVE (CAP) - PSUSA/00009305/201602

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Telaprevir - INCIVO (CAP) - PSUSA/00009306/201603

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Telavancin - VIBATIV (CAP) - PSUSA/00002879/201603

Applicant: Clinigen Healthcare Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Tobramycin (nebuliser solution)[8] - VANTOBRA (CAP) - PSUSA/00010370/201603

Applicant: PARI Pharma GmbH

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Voriconazole - VFEND (CAP) - PSUSA/00003127/201602

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Travoprost - IZBA (CAP); TRAVATAN (CAP); NAP - PSUSA/00003011/201602

Applicant: Alcon Laboratories (UK) Ltd (Izba, Travatan), various

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Acetylsalicylic acid (NAP) - PSUSA/00000039/201602

Applicant: various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Alprostadil[9] (NAP) - PSUSA/00000110/201601

Applicant: various

PRAC Lead: Eva Jirsova

Scope: Evaluation of a PSUSA procedure

[8] Centrally authorised product only
[9] Erectile dysfunction indication

Action: For adoption of recommendation to CMDh

6.3.3. Amitriptyline hydrochloride, chlordiazepoxide (NAP) - PSUSA/00000171/201602

Applicant: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Amlodipine, atorvastatin (NAP) - PSUSA/00000177/201601

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Baclofen[10] (NAP) - PSUSA/00000293/201601

Applicant: various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Bilastine (NAP) - PSUSA/00003163/201603

Applicant: various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Carboplatin (NAP) - PSUSA/00000559/201601

Applicant: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Cilostazol (NAP) - PSUSA/00010209/201602

Applicant: various

[10] Intrathecal route of administration only

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Cytomegalovirus immunoglobulin (NAP) - PSUSA/00000914/201601

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Dexamethasone (NAP) - PSUSA/00000973/201601

Applicant: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Erdosteine (NAP) - PSUSA/00001248/201602

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Ethinylestradiol, gestodene[11] (NAP) - PSUSA/00010145/201602

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Etoposide (NAP) - PSUSA/00001333/201602

Applicant: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[11] Transdermal application only

6.3.14. Exametazime, technetium (^{99m}Tc) exametazime (NAP) - PSUSA/00001344/201601

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Fluocinolone acetonide[12] (NAP) - PSUSA/00010224/201602

Applicant: various

PRAC Lead: Leonor Chambel

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Gabapentin (NAP) - PSUSA/00001499/201602

Applicant: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Glipizide (NAP) - PSUSA/00001535/201601

Applicant: various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Human coagulation factor VIII[13] (NAP) - PSUSA/00009174/201602

Applicant: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Hydrochlorothiazide; lisinopril (NAP) - PSUSA/00001654/201602

Applicant: various

[12] intravitreal implant in applicator
[13] inhibitor bypassing fraction

PRAC Lead: Margarida Guimaraes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Hydroxyethyl starch (NAP) - PSUSA/00001694/201603

Applicant: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Interferon gamma (NAP) - PSUSA/00001760/201601

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Levothyroxine (NAP) - PSUSA/00001860/201601

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Lorazepam (NAP) - PSUSA/00001909/201601

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Olodaterol (NAP) - PSUSA/00010245/201603

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Propafenone (NAP) - PSUSA/00002550/201601

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/PSUSA procedures

6.4.1. Atazanavir sulfate - REYATAZ (CAP) - EMEA/H/C/000494/LEG 083

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Claire Ferard

Scope: Submission of a comprehensive review of congenital anomalies reported with atazanavir, including a literature review and a discussion of the data gathered from the antiretroviral pregnancy registry (APR), as requested in the conclusions of PSUSA/00000258/201506 adopted by PRAC and CHMP in February 2016

Action: For adoption of advice to CHMP

6.4.2. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/LEG 047

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: Submission of a cumulative review of cases of pulmonary hypertension and a review of cases of viral reactivation as requested in the conclusions of PSUSA/00001838/201512 adopted in July 2016

Action: For adoption of advice to CHMP

6.4.3. Memantine - AXURA (CAP) - EMEA/H/C/000378/LEG 041

Applicant: Merz Pharmaceuticals GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a cumulative review of cases of hyponatremia/syndrome of inappropriate antidiuretic hormone (SIADH) as requested in the conclusions of PSUSA/H/00001967/201509 adopted in April 2016

Action: For adoption of advice to CHMP

6.4.4. Memantine - EBIXA (CAP) - EMEA/H/C/000463/LEG 041

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a cumulative review of cases of hyponatremia/syndrome of inappropriate antidiuretic hormone (SIADH) as requested in the conclusions of PSUSA/H/00001967/201509 adopted in April 2016

Action: For adoption of advice to CHMP

6.4.5. Memantine - MEMANTINE MERZ (CAP) - EMEA/H/C/002711/LEG 005

Applicant: Merz Pharmaceuticals GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a cumulative review of cases of hyponatremia/syndrome of inappropriate antidiuretic hormone (SIADH) as requested in the conclusions of PSUSA/H/00001967/201509 adopted in April 2016

Action: For adoption of advice to CHMP

6.4.6. Tadalafil - ADCIRCA (CAP) - EMEA/H/C/001021/LEG 020

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a cumulative analysis of cases of sudden hearing loss as requested in the conclusions of PSUSA/H/00002841/201510 adopted in May 2016

Action: For adoption of advice to CHMP

6.4.7. Tadalafil - CIALIS (CAP) - EMEA/H/C/000436/LEG 046

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a cumulative analysis of cases of sudden hearing loss as requested in the conclusions of PSUSA/H/00002841/201510 adopted in May 2016

Action: For adoption of advice to CHMP

6.4.8. Trastuzumab - HERCEPTIN (CAP) - EMEA/H/C/000278/LEG 098

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of a proposal for a DHPC to treating oncologists and/or oncologists to ensure awareness of the need to follow the current guidance on cardiac monitoring during and after completion of treatment with Herceptin and to highlight the need for cardiac monitoring during handover of patient management to other physicians as requested in the conclusions of EMEA/H/C/PSUSA/00003010/201509 adopted in April 2016

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

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

7.1.1. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/PSP/004

Applicant: GlaxoSmithKline Trading Services, ATMP[15]

PRAC Rapporteur: Sabine Straus

Scope: PASS protocol for study GSK2696273 entitled 'adenosine deaminase severe combined immunodeficiency (ADA-SCID) registry for patients treated with Strimvelis gene therapy: long-term prospective, non-interventional follow-up of safety and effectiveness'

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

7.1.2. Levonorgestrel (NAP) - EMEA/H/N/PSA/j/0006.1

Applicant: Bayer Pharma AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Revised PASS protocol for study EURAS-LCS12: a European active surveillance study of LCS-12, an intra-uterine device (IUD) for Jaydess and Luadei (levonorgestrel) to assess among new users the risks of certain events associated with the use of LCS-12 compared to established IUDs or IUSs (intra-uterine system) during standard clinical practice and to describe drug utilisation patterns as per the request for supplementary information adopted in May 2016

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[16]

7.2.1. Fenofibrate, simvastatin - CHOLIB (CAP) - EMEA/H/C/002559/MEA 002.4

Applicant: BGP Products Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 002.2: revised PASS protocol for study ABT285.E.001: a drug utilisation research (DUR) study on the use of fenofibrate and simvastatin fixed combination: a European multinational study using secondary health records databases, as per the request for supplementary information (RSI) adopted in February 2016

[14] In accordance with Article 107n of Directive 2001/83/EC
[15] Advanced Therapy Medicinal Product
[16] 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

7.2.2. Florbetaben (^{18}F) - NEURACEQ (CAP) - EMEA/H/C/002553/MEA 001.4

Applicant: Piramal Imaging Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA. 001.3: revised PASS protocol for study FBB-01_03_13 (PASS2): a non-interventional prospective observational multicentre, multinational registry to observe usage pattern, safety and tolerability of the diagnostic agent NeuraCeq in clinical practice as per the request for supplementary information (RSI) adopted in September 2015

Action: For adoption of advice to CHMP

7.2.3. Follitropin alfa - OVALEAP (CAP) - EMEA/H/C/002608/MEA 002.2

Applicant: Teva B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA. 002.2: revised PASS protocol XM17-WH-50005: SOFIA - safety of Ovaleap in infertile women undergoing superovulation for assisted reproductive technologies, a multinational, comparative, prospective, non-interventional, observational cohort study as per the request for supplementary information (RSI) adopted in February 2015

Action: For adoption of advice to CHMP

7.2.4. Naltrexone, bupropion - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.1

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Revised PASS protocol for a drug utilisation study (DUS): a retrospective chart review and nested naltrexone/bupropion (NB) prescribing physician cross sectional survey to include a multicentre research programme of observational studies to monitor safety and drug utilisation and the MAH's response to the request for supplementary of information (RSI) as adopted in November 2015

Action: For adoption of advice to CHMP

7.2.5. Naltrexone, bupropion - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 004.1

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of a revised PASS protocol for the naltrexone/bupropion observational database study to include a multicentre research programme of observational studies to monitor safety and drug utilisation with the MAH's response to MEA 003 on naltrexone/bupropion (NB) drug utilisation study (DUS): a retrospective chart review and

nested NB prescribing physician cross sectional survey as adopted in November 2015

Action: For adoption of advice to CHMP

7.2.6. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/MEA 008.2

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's responses to MEA 008 on a protocol for study CA209234: a non-interventional category 3 PASS: pattern of use, safety, and effectiveness of nivolumab in routine oncology practice as per the request for supplementary information (RSI) adopted in March 2016

Action: For adoption of advice to CHMP

7.2.7. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 001

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Rafe Suvarna

Scope: Submission of a protocol for a non-interventional non-imposed PASS: observational cohort study of pulmonary arterial hypertension (PAH) patients exposed and unexposed to selexipag in routine clinical practice

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[17]

None

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

7.4.1. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/II/0040

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study report of the AEGEAN study (CV185-220) assessing the education and guidance programme for Eliquis (apixaban) adherence in non-valvular atrial fibrillation patients. The RMP is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Bivalirudin - ANGIOX (CAP) - EMEA/H/C/000562/II/0068

Applicant: The Medicines Company UK Ltd.

[17] In accordance with Article 107p-q of Directive 2001/83/EC
[18] 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

PRAC Rapporteur: Julie Williams

Scope: Submission of the final results of the drug utilisation study Eurovision 2. The RMP is amended to refine the additional risk minimisation measures in line with the findings of the study

Action: For adoption of PRAC Assessment Report

7.4.3. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/II/0040

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Claire Ferard

Scope: Submission of the results for PASS study Instanyl-5001: an evaluation of the effectiveness of risk minimisation measures: a survey among health care professionals to assess their knowledge and attitudes on prescribing conditions of Instanyl in France and the Netherlands included in the RMP

Action: For adoption of PRAC Assessment Report

7.4.4. Pioglitazone - ACTOS (CAP) - EMEA/H/C/000285/WS0990/0074; GLUSTIN (CAP) - EMEA/H/C/000286/WS0990/0072 pioglitazone, glimepiride - TANDEMACT (CAP) -EMEA/H/C/000680/WS0990/0050; pioglitazone, metformin - COMPETACT (CAP) - EMEA/H/C/000655/WS0990/0061; GLUBRAVA (CAP) - EMEA/H/C/000893/WS0990/0046

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: Submission of the final drug utilisation study report (Pioglitazone_5019) conducted in Denmark designed to assess the utilisation of pioglitazone in Denmark after July 2011 when labelling changes were introduced following the conclusion of an Article 20 procedure

Action: For adoption of PRAC Assessment Report

7.4.5. Pioglitazone - ACTOS (CAP) - EMEA/H/C/000285/WS0991/0075; GLUSTIN (CAP) - EMEA/H/C/000286/WS0991/0073 pioglitazone, glimepiride - TANDEMACT (CAP) - EMEA/H/C/000680/WS0991/0051 pioglitazone, metformin - COMPETACT (CAP) - EMEA/H/C/000655/WS0991/0062; GLUBRAVA (CAP) - EMEA/H/C/000893/WS0991/0047

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: Submission of the final study report for the Clinical Practice Research Datalink (CPRD) GOLD linkage study (Pioglitazone_5018) conducted to investigate a possible association of the use of pioglitazone with prostate cancer and data on the incidence of adjudicated prostate cancer in patients receiving pioglitazone in the long-term insulin resistance intervention after stroke (IRIS) trial

Action: For adoption of PRAC Assessment Report

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

7.5.1. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 006.1

Applicant: Hexal AG

PRAC Rapporteur: Julie Williams

Scope: Fifth annual interim safety report for study EP006-401: safety follow-up of severe chronic neutropenia (SCN) patients included in phase IV study: safety data will be collected via cooperation with the Severe Chronic Neutropenia International Registry and reported annually

Action: For adoption of advice to CHMP

7.5.2. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 006.1

Applicant: Hexal AG

PRAC Rapporteur: Julie Williams

Scope: Fifth annual interim safety report for study EP006-401: safety follow-up of severe chronic neutropenia (SCN) patients included in phase IV study: safety data will be collected via cooperation with the Severe Chronic Neutropenia International Registry and reported annually

Action: For adoption of advice to CHMP

7.5.3. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.2

Applicant: Hexal AG

PRAC Rapporteur: Julie Williams

Scope: Fifth annual interim report for study EP06-501 after four years of treatment: a non-interventional, prospective, long-term observational study to assess the safety and effectiveness of Zarzio/Filgrastim Hexal administered to healthy unrelated stem cell donors for peripheral blood progenitor cell mobilisation

Action: For adoption of advice to CHMP

7.5.4. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.2

Applicant: Hexal AG

PRAC Rapporteur: Julie Williams

Scope: Fifth annual interim report for study EP06-501 after four years of treatment: a non-interventional, prospective, long-term observational study to assess the safety and effectiveness of Zarzio/Filgrastim Hexal administered to healthy unrelated stem cell donors for peripheral blood progenitor cell mobilisation

Action: For adoption of advice to CHMP

7.5.5. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 026.2

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: First progress report for study MRK-2859: ulcerative colitis (UC) Nordic registry: a non-interventional observational longitudinal PASS of Simponi in the treatment of UC using Nordic national health registries

Action: For adoption of advice to CHMP

7.5.6. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/MEA 008.3

Applicant: Hospira UK Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Annual report for the post marketing surveillance of Inflectra/Remsima 100 mg to evaluate safety and efficacy in Korea

Action: For adoption of advice to CHMP

7.5.7. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 008.3

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Rafe Suvarna

Scope: Annual report for the post marketing surveillance of Inflectra/Remsima 100 mg to evaluate safety and efficacy in Korea

Action: For adoption of advice to CHMP

7.5.8. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - OPTAFLU (CAP) - EMEA/H/C/000758/MEA 041.5

Applicant: Novartis Influenza Vaccines Marburg GmbH

PRAC Rapporteur: Menno van der Elst

Scope: PASS interim results for study V58_30OB: an observational study to investigate the safety of Optaflu vaccination in adults in routine clinical care in the UK using the Health Improvement Network (THIN) database

Action: For adoption of advice to CHMP

7.5.9. Nomegestrol, estradiol - ZOELY (CAP) - EMEA/H/C/001213/ANX 011.2

Applicant: Teva B.V.

PRAC Rapporteur: Claire Ferard

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)

7.5.10. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/MEA 265.6

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Claire Ferard

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

Action: For adoption of advice to CHMP

7.5.11. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.11

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Annual report for study PSOLAR (PSOriasis Longitudinal Assessment and Registry), an international prospective cohort study/registry programme designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/MEA 011.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's responses to MEA 011.4 on a feasibility assessment and proposal for an alternative approach to achieve relevant data of incidence of pancreatic cancer for study B017, an observational study using one or more European databases to investigate incidence of pancreatic cancers and thyroid neoplasms among type 2 diabetes mellitus patients who initiate therapy with exenatide once weekly as per the request for supplementary information adopted in June 2015

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Clofarabine - EVOLTRA (CAP) - EMEA/H/C/000613/S/0050 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Claire Ferard

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. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/R/0007 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - EMEA/H/C/002450/R/0008 (with RMP)

Applicant: Chiesi Farmaceutici S.p.A., ATMP[19]

PRAC Rapporteur: Julie Williams

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Capecitabine - ECANSYA (CAP) - EMEA/H/C/002605/R/0018 (without RMP)

Applicant: Krka, d.d., Novo mesto

PRAC Rapporteur: Martin Huber

[19] Advanced Therapy Medicinal Product

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Pioglitazone - PIOGLITAZONE TEVA (CAP) - EMEA/H/C/002297/R/0016 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Pioglitazone - PIOGLITAZONE TEVA PHARMA (CAP) - EMEA/H/C/002410/R/0013 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Pioglitazone hydrochloride - PIOGLITAZONE ACCORD (CAP) - EMEA/H/C/002277/R/0011 (without RMP)

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Telbivudine - SEBIVO (CAP) - EMEA/H/C/000713/R/0045 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Zoledronic acid - ZOLEDRONIC ACID ACTAVIS (CAP) - EMEA/H/C/002488/R/0017 (without RMP)

Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Doris Stenver

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Guanfacine – INTUNIV (CAP) - EMEA/H/C/003759/II/0004

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: PRAC consultation on a variation to update sections 4.2, 4.4 and 4.8 of the SmPC to include a warning and update the safety information as a result of a post-marketing case of hypertensive encephalopathy upon abrupt discontinuation of Intuniv

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

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

11.1. Safety related variations of the marketing authorisation

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

Applicant: Bioprojet Europe Ltd (Hidrasec)

PRAC Lead: Qun-Ying Yue

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

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

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

Action: For discussion

12.3.2. Scientific Advice Working Party (SAWP) – pilot phase on involving the PRAC in non-imposed PASS protocols: objectives and impact

Action: For discussion

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. 2017 PRAC work plan – preparation

PRAC lead: June Raine

Action: For discussion

12.8. Planning and reporting

12.8.1. Marketing authorisation applications (MAA) - planned for the remainder of 2016

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Margarida Guimarães

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Sabine Straus

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

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

None

12.13.2. EudraVigilance Access Policy – update

Action: For adoption

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Good Pharmacovigilance Practice (GVP) Module V on risk management systems

Action: For adoption

12.14.2. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. EMA industry platform on the operation of the EU pharmacovigilance legislation – feedback from the ninth meeting on 21 September 2016

Action: For discussion

12.20.2. EMA stakeholders forum on the implementation of the pharmacovigilance legislation – feedback from the tenth meeting on 21 September 2016

Action: For discussion

12.20.3. Good Pharmacovigilance Practice (GVP) Guideline on product or population specific considerations III: pregnancy and breastfeeding

Action: For discussion

12.20.4. Initial marketing authorisation application (MAA) procedures: early background summaries – review of experience

Action: For discussion

13. Any other business

14. Explanatory notes

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

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

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

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

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

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

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

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

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

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

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

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

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

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