6 March 2017
EMA/PRAC/159496/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 6-9 March 2017

Chair: June Raine – Vice-Chair: Almath Spooner

6 March 2017, 13:00 – 19:30, room 3/A

7 March 2017, 08:30 – 19:30, room 3/A

8 March 2017, 08:30 – 19:30, room 3/A

9 March 2017, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

23 March 2017, 09:00 – 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 scope listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also change during the course of the review. Additional details on some of these procedures will be published in the PRAC meeting highlights once the procedures are finalised.

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

Note on access to documents

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

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

Table of contents

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 6-9 March 2017. See March 2017 PRAC minutes (to be published post April 2017 PRAC meeting).

1.2. Adoption of agenda of the meeting on 6-9 March 2017

Action: For adoption

1.3. Adoption of the minutes of the previous meeting on 6-9 February 2017

Action: For adoption

2. EU referral procedures for safety reasons: urgent EU procedures

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

2.4. Planned public hearings

None

3. EU referral procedures for safety reasons: other EU referral procedures

3.1. Newly triggered procedures

3.1.1. Valproate and related substances: sodium valproate, valproic acid, valproate semisodium, valpromide (NAP)

Applicant: Sanofi-Aventis, various

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

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

Action: For adoption of a list of questions

3.2. Ongoing procedures

3.2.1. Lactose of bovine origin-containing medicinal products[1]: methylprednisolone (NAP) - EMEA/H/A-31/1449

Applicant: Pfizer Croatia d.o.o. (Solu-Medrol), various

PRAC Rapporteur: Jan Neuhauser; PRAC Co-rapporteur: Nikica Mirošević Skvrce

Scope: Review of the benefit-risk balance following notification by Croatia 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)

3.2.2. Paracetamol[2] (NAP) - EMEA/H/A-31/1445

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

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

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

Action: For adoption of a list of outstanding issues (LoOI)

[1] For intravenous (IV) or intramuscular (IM) use indicated for the treatment of acute allergic reactions only
[2] Modified release formulations

3.2.3. 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: Ana Sofia Diniz Martins; 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 following the targeted meeting with patients and healthcare professionals (HCPs)

3.3. Procedures for finalisation

3.3.1. 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)

Applicant: Mallinckrodt Deutschland GmbH (Optimark); various

PRAC Rapporteur: Patrick Batty; 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 recommendation to CHMP

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

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

PRAC Rapporteur: Julie Williams; PRAC Co-rapporteur: Brigitte Keller-Stanislawski

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

Action: For adoption of a recommendation to CHMP

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

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Fulvestrant - FASLODEX (CAP)

Applicant: AstraZeneca UK Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of anaphylactic reactions

Action: For adoption of PRAC recommendation

EPITT 18832 – New signal

Lead Member State: SE

4.1.2. Docetaxel – TAXOTERE (CAP), DOCETAXEL ACCORD (CAP), TAXESPIRA (CAP)

Applicant(s): Aventis Pharma S.A. (Taxotere), Accord Healthcare Ltd (Docetaxel Accord), Hospira UK Limited (Taxespira), various

PRAC Rapporteur: Claire Ferard

Scope: Signal of unexpected seriousness of reported adverse drug reactions with docetaxel and suspicion of an increase in adverse drug reactions (ADR) reporting rate in France with docetaxel-containing products

Action: For adoption of PRAC recommendation

EPITT 12059 – New signal

Lead Member State: FR

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Ciprofloxacin (NAP); meropenem (NAP)

Applicant(s): various

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

PRAC Rapporteur: Jan Neuhauser

Scope: Signal of incompatibility leading to possible precipitation when co-administered intravenously

Action: For adoption of PRAC recommendation

EPITT 18790 – Follow-up to December 2016

4.3.2. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/SDA/012

Applicant(s): Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Signal of hepatotoxicity

Action: For adoption of PRAC recommendation

EPITT 18754 – Follow-up to November 2016

4.3.3. Loperamide (NAP)

Applicant(s): various

PRAC Rapporteur: Andri Andreou

Scope: Signal of serious cardiac events with high doses of loperamide from abuse and misuse

Action: For adoption of PRAC recommendation

EPITT 18339 – Follow-up to July 2016

4.3.4. Nivolumab - OPDIVO (CAP)- EMEA/H/C/003985/SDA/015; pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/011

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

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of transplant rejection

Action: For adoption of PRAC recommendation

EPITT 18781 – Follow-up to November 2016

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Alpha-1-antitrypsin - EMEA/H/C/003934, Orphan

Applicant: Kamada BioPharma Limited at Fieldfisher LLP

Scope: Treatment and maintenance therapy of adult patients with congenital deficiency of alpha-1 antitrypsin and lung disease with clinical evidence of emphysema and airway obstruction (forced expiratory volume in 1 second (FEV1)/slow vital capacity (SVC) <70%)

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

5.1.2. Dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171

Scope: Prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4

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

5.1.3. Efavirenz, emtricitabine, tenofovir disoproxil –EMEA/H/C/004250

Scope: Treatment of human immunodeficiency virus (HIV)-1 infection

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

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

Scope: Treatment of breast cancer with brain metastases

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

5.1.5. Nitisinone - EMEA/H/C/004281

Scope: Treatment of hepatorenal tyrosinemia type 1

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

5.1.6. Ocrelizumab - EMEA/H/C/004043

Scope: Treatment of multiple sclerosis

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. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/WS1103/0018; XIGDUO (CAP) - EMEA/H/C/002672/WS1103/0029

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 8.3) to implement the outcome of the Article 31 referral procedure (EMEA/H/A-31/1432) on metformin and metformin-containing medicines regarding the use in patients with moderate renal impairment (Commission Decision dated 12 December 2016)

Action: For adoption of PRAC Assessment Report

5.2.2. Darunavir - PREZISTA (CAP) - EMEA/H/C/000707/WS1059/0084; Darunavir, cobicistat - REZOLSTA (CAP) - EMEA/H/C/002819/WS1059/0015

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 3.1) in order to delete the category 3 study TMC114HIV3015: a single arm, open label trial to assess the pharmacokinetics of darunavir/ritonavir, darunavir/cobistat, etravirine and rilpivirine in human immunodeficiency virus (HIV)-1 infected pregnant women, and replace it by pharmacokinetics data in HIV-1 pregnant women

Action: For adoption of PRAC Assessment Report

5.2.3. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/WS1063/0022; Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/WS1063/0027

Applicant: AbbVie Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the RMP for Exviera and Viekirax to: 1) add information on cases of hepatic decompensation observed in patients with Child-Pugh B hepatic impairment, and to reflect the changes of the SmPC to change the dose recommendation of these patients to 'not recommended', as well as the addition of statements recommending the monitoring of hepatic function in these patients as approved on WS/0873; 2) add a reference to nine drug-drug interaction studies as approved in WS0896/G; 3) include a reference to the completion of rat 2 year carcinogenicity studies as recently approved in variations II-06 (Exviera) and II-04 (Viekirax) respectively; 4) reflect the update of section 4.2 of SmPC for Viekirax to recommend a decrease in treatment duration of 12 weeks in genotype 4 (GT4) cirrhotic patients, with a consequential change to sections 4.4 and 5.1 as approved in II-22-G; 5) remove the non-clinical PAMS 1-3,(MEA/003, MEA/002, MEA/003)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/II/0107

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information following the MAH's initiative to update its clinical trials safety database to include all currently completed clinical trials for both the intravenous (IV) and subcutaneous (SC) formulations. The adverse reactions' table in section 4.8 as well as the description of selected adverse reactions of special interest is amended. As a consequence, section 4.4 is brought in line with the amended section 4.8. The Package Leaflet and the RMP (version 22) are updated accordingly

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

5.3.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0163

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of chronic non-infectious uveitis in paediatric patients. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated accordingly. In addition, the MAH took the opportunity to implement an alternative format statement for blind/partially sighted patients into the Package Leaflet as introduced with procedure EMEA/H/C/000481/N/0155. Furthermore, the MAH made some editorial changes to the package leaflet

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

5.3.3. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0047

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report for study LBSL99/BEL112626 (RMP, category 3, MEA 010): a multicentre, open label, continuation trial of monoclonal anti-BLyS antibody in subjects with systemic lupus erythematosus (SLE) who completed the phase 2 protocol LBSL02. The RMP (version 22) is updated accordingly

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

5.3.4. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0012

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include Zykadia as first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated to update the information based primarily on the supporting study CLDK378A2301 (ASCEND-4: a phase III multicentre, randomized study of oral ceritinib versus standard chemotherapy in previously untreated adult patients with ALK rearranged (ALK-positive), stage IIIB or IV, non-squamous NSCLC). The Package Leaflet and the RMP (version 6.0) are updated accordingly

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

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped applications including: 1) line extension to introduce a new pharmaceutical form associated with new strengths (1 mg, 2.5 mg and 5 mg hard capsules), 2) 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, Labelling and the RMP (version 7.0) 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

5.3.6. Cobicistat - TYBOST (CAP) - EMEA/H/C/002572/WS1086/0034 Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - EMEA/H/C/002574/WS1086/0077

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report for study GS-US-236-0140: a phase IV, randomized, open-label study evaluating the renal effect of elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (DF) or other tenofovir DF-containing regimens (ritonavir-boosted atazanavir plus emtricitabine/tenofovir DF or efavirenz/emtricitabine/tenofovir DF) compared to ritonavir-boosted atazanavir plus abacavir/lamivudine in antiretroviral treatment-naïve human immunodeficiency virus (HIV)-1 infected adults with an estimated glomerular filtration rate (eGFR)≥70 mL/min. The RMP (version 2.0) is updated accordingly

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

5.3.7. Darunavir - PREZISTA (CAP) - EMEA/H/C/000707/WS1089/0086/G; Darunavir, cobicistat - REZOLSTA (CAP) - EMEA/H/C/002819/WS1089/0018/G

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variation including: 1) submission of the final report for study GS-US-236-0140 (RMP, category 3): a phase IV, randomized, open-label study evaluating the renal effect of elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (DF) or other tenofovir DF-containing regimens (ritonavir-boosted atazanavir plus emtricitabine/tenofovir DF or efavirenz/emtricitabine/tenofovir DF) compared to ritonavir-boosted atazanavir plus abacavir/lamivudine in antiretroviral treatment-naïve human immunodeficiency virus (HIV)-1 infected adults with an estimated glomerular filtration rate (eGFR)≥70 mL/min. The RMP (version 25.0 for Prezista and version 4.0 for Rezolsta) are updated accordingly. The RMP are also updated to remove the important potential risks of 'renal toxicity'.; 2) based on a cumulative review of the available data, the RMPs are also updated to remove the important risks of 'pancreatis', 'convulsions' and 'cardiac conduction abnormalities' and the important risk 'development of drug resistance'

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

5.3.8. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0086/G, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations including: 1) update of section 4.8 of the SmPC with the adverse drug reactions (ADR) frequencies to reflect overall exposure to eculizumab in clinical trials; 2) update of section 4.4 of the SmPC with warning and precautions on meningococcal vaccination timing as recommended by PRAC. The Package Leaflet, Annex II and the RMP (version 13) are updated accordingly. In addition, the RMP is updated in order to implement the previous PRAC recommendation to remove the off label use from missing information, to provide the exposure data from PSUR#13 and to update the epidemiology sections with more complete and recent scientific literature data. Moreover, the MAH took the opportunity to update the Product Information to add editorial changes and to bring it in line with the latest QRD template

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

5.3.9. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0090, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include the 'treatment of refractory generalised myasthenia gravis (gMG) patients who are antiacetylcholine receptor (AChR) antibody-positive'. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated to include information on the new indication and to include the new methodology to calculate the adverse drug reaction frequencies in section 4.8. The RMP (version 14.0) is updated accordingly

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

5.3.10. Elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - EMEA/H/C/004042/II/0026

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include paediatric patients from 6 to less than 12 years of age, with a body weight of at least 25kg, infected with human immunodeficiency virus (HIV)-1 without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir. As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on the analysis of the paediatric study GS-US-292-0106 (cohort 2): a phase 2/3, open-label study of the pharmacokinetics, safety, and antiviral activity of the elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) single tablet regimen (STR) in HIV-1 Infected antiretroviral treatment naive adolescents and virologically suppressed children. The Package Leaflet and the RMP (version 3) are updated accordingly

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

5.3.11. Emtricitabine, tenofovir disoproxil – EMTRICITABINE,TENOFOVIR DISOPROXIL MYLAN (CAP) - EMEA/H/C/004050/II/0001

Applicant: Mylan S.A.S

PRAC Rapporteur: Julie Williams

Scope: Update of the SmPC following the assessment of the extension of indication for the reference product, Truvada, for pre-exposure prophylaxis. The Package Leaflet, Annex II and Labelling are updated accordingly

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

5.3.12. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/II/0034

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of section 5.1 of the SmPC in order to reflect the final results of the post authorisation efficacy study (PAES) CL-9785-0410 which was a study of enzalutamide in patients with progressive mCRPC previously treated with abiraterone acetate, listed as a category 3 in the RMP. The RMP (version 11.0) is updated accordingly

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

5.3.13. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/II/0035

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.4 and 4.8 of the SmPC to reflect the final results of PASS CL-9785-0403 (UPWARD): a multicentre, single-arm, open-label, post-marketing safety study to evaluate the risk of seizure among subjects with metastatic castration-resistant prostate cancer (mCRPC) treated with enzalutamide who are at potential increased risk of seizure (RMP category 3). The RMP (version 11.0) is updated accordingly. In addition, the MAH took the opportunity to introduce a correction in section 5.1 of the SmPC

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

5.3.14. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/II/0036

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.6 and 5.3 of the SmPC to reflect the final results of study AE-7592-G on transfer of radioactivity into foetuses and breast milk in rats after a single oral administration of [^{14}C] enzalutamide - ISN: 9785-ME-0046. The Package Leaflet and the RMP (version 11.0) are updated accordingly

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

5.3.15. Eslicarbazepine acetate - ZEBINIX (CAP) - EMEA/H/C/000988/II/0053

Applicant: Bial - Portela & Cª, S.A.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include the use of Zebinix as monotherapy in adults, in addition to the previously authorised indication as adjunctive therapy. As a consequence,

sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 15.0) are updated accordingly. In addition, the MAH claims an additional 1-year period of market protection under Article 14(11) of Regulation (EC) No 726/2004

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

5.3.16. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0041

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 4.1 of the SmPC in order to align it with more recently approved glucose-lowering agents and with the 'reflection paper on the wording of indication for medicinal products for treatment of type 2 diabetes' In addition, update of section 5.1 based on study D5553C00003 (Duration 8 study): a 28-week, multicentre, randomized, double-blind, active-controlled, Phase 3 study with a 24-week extension phase followed by a 52-week extension phase to evaluate the efficacy and safety of simultaneous administration of exenatide once weekly 2 mg and dapagliflozin once daily 10 mg compared to exenatide once weekly 2 mg alone and dapagliflozin once daily 10 mg alone in patients with type 2 diabetes who have inadequate glycemic control on metformin. The Package Leaflet and the RMP (version 24) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes in the SmPC and Package Leaflet

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

5.3.17. Fampridine - FAMPYRA (CAP) - EMEA/H/C/002097/II/0036/G

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Sabine Straus

Scope: Grouped variations to: 1) update sections 4.2 and 5.1 of the SmPC, Annex II and the Package Leaflet based on the results of the clinical study ENHANCE: a multicentre, randomized, double blind, placebo controlled study to assess the long-term efficacy and safety of prolonged release fampridine 10 mg, administered twice daily in subjects with multiple sclerosis; 2) update of section 4.6 of the SmPC based on the data from pregnancy registry; 3) update of section 4.2 and 5.2 of the SmPC based on the core data sheet (CDS) and PRAC review of the Fampyra PSUR#03. The RMP (version 11) is updated accordingly. In addition, the MAH took the opportunity to bring the Product Information in line with the latest QRD template (version 10.0). Finally, a switch from a conditional to a standard marketing authorisation (MA) is assessed as part of this procedure

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

5.3.18. Follitropin delta - REKOVELLE (CAP) - EMEA/H/C/003994/II/0003/G

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations including: 1) introduction of a pre-filled cartridge as a new presentation for Rekovelle strength 12 µg/0.36mL; 2) addition of a new pack size for the strength 36 µg/1.08mL and addition of a new pack size for the strength 72 µg/2.16mL. As a

consequence, sections 2, 4.2, 6.3, 6.5, 6.6 and 8 of the SmPC are updated. The Package Leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.19. Human coagulation factor VIII, human von Willebrand factor - VONCENTO (CAP) - EMEA/H/C/002493/II/0017/G

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sabine Straus

Scope: Grouped variations including: 1) update of section 4.8 of the SmPC in order to amend the frequencies of undesirable effects to reflect the final clinical study report (CSR) from study CSLCT-BIO-08-53: a phase III, open-label, multicentre study to evaluate efficacy, pharmacokinetics, and safety of Voncento in paediatric subjects with haemophilia A. The Package Leaflet and the RMP (version 6.1) are updated accordingly. The revised RMP also includes the removal of the commitment to conduct a post-marketing study for haemophilia A patients (study CSLCT-BIO-12-78) for Voncento as a consequence of new data from study CSLCT-BIO-08-53. In addition, the MAH took the opportunity to combine different strengths in the SmPC and Package Leaflet

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

5.3.20. Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - GARDASIL (CAP) - EMEA/H/C/000703/WS1128/0071; SILGARD (CAP) - EMEA/H/C/000732/WS1128/0062

Applicant: Sanofi Pasteur MSD SAS

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 5.1 of the SmPC based on the final report for study P019-21: a long-term follow-up study of safety, immunogenicity, and effectiveness of human papillomavirus [types 6, 11, 16, 18] recombinant vaccine in mid-adult women (FUTURE III (females united to unilaterally reduce endo-/ecto-cervical cancer)) (Gardasil MEA 060.2; Silgard MEA 059.2) and fourth interim report for study P015-21: a registry-based study of protocol V501-015 subjects, and recipients of human papillomavirus [types 6, 11, 16, 18] recombinant vaccine in countries with centralised cervical cancer screening infrastructures to evaluate the long-term effectiveness, immunogenicity, and safety of human papillomavirus [types 6, 11, 16, 18] recombinant vaccine (Gardasil/Silgard MEA 019.7). The RMP (version 11) is updated accordingly

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

5.3.21. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0204

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final registry report from C0168T71 study: a review and analysis of birth outcomes from Swedish, Danish and Finish medical birth registers and an evaluation of pregnancy data from multiple sources. Section 4.6 of the SmPC, the Package Leaflet and

the RMP (version 13.2) are updated accordingly. The MAH also took the opportunity to bring the product information in line with the QRD template and update the local representatives of the Package Leaflet

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

5.3.22. Insulin degludec - TRESIBA (CAP) - EMEA/H/C/002498/II/0024/G

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations to update sections 4.2 and 5.1 of the SmPC in order to include updated information on the use of Tresiba in terms of transfer from other basal insulin regimens and the effects of Tresiba on hypoglycaemia following the completion of studies NN1250-3995 (SWITCH 1: a randomised, double blind, cross-over trial comparing the safety and efficacy of insulin degludec and insulin glargine, both with insulin aspart as mealtime insulin in subjects with type 1 diabetes) and NN1250-3998 (SWITCH 2: a randomised, double blind, cross-over trial comparing the safety and efficacy of insulin degludec and insulin glargine, with or without oral antidiabetic drugs in subjects with type 2 diabetes), comparing the safety and efficacy of Tresiba (insulin degludec) and insulin glargine U-100. The Package Leaflet, Labelling and RMP (version 7.0) are updated accordingly. The MAH took the opportunity to bring the Product Information in line with the latest QRD template (version 10). Finally, minor changes have been made to the SmPC section 4.2 and the corresponding section of the Package Leaflet to clarify the correct use of Tresiba (insulin degludec)

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

5.3.23. Insulin degludec, liraglutide - XULTOPHY (CAP) - EMEA/H/C/002647/II/0017

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.2 of the SmPC in order to update the information on use of Xultophy in patients with hepatic impairment based on clinical trial NN2211-1328 (a single-centre, open-label trial investigating the pharmacokinetics and the safety profile after a single dose of liraglutide in subjects with hepatic impairment and in subjects with normal hepatic function), the LEAD 1-6 meta-analysis as well as other liraglutide trials. In addition, 'fatigue' has been added to the tabulated list of adverse reactions in section 4.8 of the SmPC. The Package Leaflet and the RMP (version 6.0) are updated accordingly. 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

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

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations to: 1) update sections 4.4, 4.8, and 5.1 of the SmPC in order to

add a warning on QTc prolongation and update safety information following the submission of study report EGF114271: a phase IV placebo controlled single sequence crossover study to evaluate the effect of repeat oral doses of lapatinib on cardiac repolarization in patients with advanced cancer; 2) update section 4.8 of the SmPC in order to further elaborate on the undesirable effect 'serious cutaneous reactions' based on the review of the MAH's safety database. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the product information (PI) in line with the latest QRD template (version 10) and to update Annex II to delete a condition which was fulfilled with procedure ANX 28.2. The RMP (version 32) is updated accordingly also introducing template-related changes, study milestones updates, and to upgrade 'food effect' to an important identified risk (from procedure EMEA/H/C/000795/II/0024)

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

5.3.25. Nilotinib - TASIGNA (CAP) - EMEA/H/C/000798/X/0088/G, Orphan

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Grouped application including: 1) extension of indication to include the treatment of paediatric patients with newly diagnosed Philadelphia chromosome-positive chronic myelogenous leukaemia in chronic phase (Ph+ CML-CP), or with Ph+ CML-CP resistant or intolerant to prior therapy including imatinib, based on results from two clinical studies in paediatric patients conducted in accordance with the approved Tasigna paediatric investigation plan (PIP): a phase I pharmacokinetic (PK) study CAMN107A2120 (a multicentre, open-label, pharmacokinetic study of oral nilotinib in paediatric patients with newly diagnosed chronic phase (CP) Ph+ CML, with CP or accelerated phase (AP) Ph+ CML resistant/intolerant to imatinib and/or dasatinib, or with refractory/relapsed Ph+ ALL) and a Phase II safety and efficacy study CAMN107A2203 (a multicentre, open label, non-controlled phase II study to evaluate efficacy and safety of oral nilotinib in paediatric patients with newly diagnosed Ph+ CML in CP or with Ph+ CML in CP or AP resistant or intolerant to either imatinib or dasatinib). The RMP (version 18.0) is updated accordingly; 2) line extension to add a new strength of 50mg hard capsules. In addition, the MAH proposed to merge the SmPCs for the 50 mg and 200 mg strengths

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

5.3.26. 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

5.3.27. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0029

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of hepatocellular carcinoma after prior sorafenib therapy in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP (version 8.0) are updated accordingly

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

5.3.28. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0030

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of adults with mismatch repair deficient (dMMR) or microsatellite instability high (MSI-H) metastatic colorectal cancer after prior fluoropyrimidine based therapy. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated in order to add the new indication and update the safety information. The Package Leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.29. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0014

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of classical Hodgkin lymphoma (cHL) in adults who have refractory disease, or who have relapsed after greater than 3 prior lines of therapy, based on the results from study KEYNOTE-087, an open-label phase II trial of pembrolizumab in subjects with relapsed or refractory cHL and study KEYNOTE-013, a phase Ib multi-cohort trial of pembrolizumab in subjects with hematologic malignancies. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 5.0) are updated accordingly

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

5.3.30. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/II/0004/G, Orphan

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations to update sections 4.4, 4.5, 4.6 and 5.2 of the SmPC based on the final clinical study report (CSR) of study P15-02 assessing the mass balance recovery, metabolite profile and metabolite identification of [^{14}C]-pitolisant at steady state conditions, in healthy cytochrome P450 2D6 (CYP2D6) phenotyped subjects, study P14-07 evaluating

the pharmacokinetic interaction of pitolisant with sodium oxybate and modafinil in healthy male volunteers and study P15-15 evaluating the pharmacokinetic (PK) interaction of pitolisant with cytochrome P450 3A4 (CYP3A4) substrates (midazolam), cytochrome P450 2B6 (CYP2B6) substrates (bupropion), UDP-Glucuronosyltransferase-2B7 (UGT2B7) inhibitors (probenecide)) in fulfilment of PAM (MEA 02, 03 and 04). The Package Leaflet and the RMP (version 5.0) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial change in section 4.8 of the SmPC

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

5.3.31. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/II/0005/G

Applicant: Teva Pharmaceuticals Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations including an update of section 4.2 of the SmPC in order to include a revised dosing regimen as a result of the new 2 5mg vial presentation. As a consequence, update of sections 6.5 and 6.6 of the SmPC to change the pack size of the finished product. The Annex II, Package Leaflet, Labelling and RMP (version 2.0) are updated accordingly

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

5.3.32. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/II/0060/G, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations including: 1) extension of indication to include paediatric population to register Nplate for the use in the paediatric chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients from 1 year of age and older. As a consequence, sections 1, 2, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 6.3 6.5, 6.6 and 8 of the SmPC are updated accordingly. The RMP (version 18) is updated accordingly. Furthermore, the Product information is brought in line with the latest QRD template (version 10); 2) addition of a low-dose romiplostim 125 microgram vial presentation for powder for solution for injection (4 vials pack); 3) addition of a 1 vial pack size of a low-dose romiplostim 125 microgram presentation

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

5.3.33. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS1075/0037; Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/WS1075/0006; Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/WS1075/0043

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final non-clinical study report PC-334-2035 assessing the potential for a pharmacokinetic (PK) interaction via transporter or enzyme based inhibition when sofosbuvir and other direct acting antivirals (DAAs) are used concomitantly with amiodarone. The RMPs (version 1.0 for Epclusa, version 2.0 for Harvoni, version 5.0 for

Sovaldi) are updated accordingly

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

5.3.34. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0066

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the use in adult patients for the treatment of giant cell arteritis for the subcutaneous formulation of RoActemra. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated to reflect information relevant to this indication. The Package Leaflet and the RMP (version 21) are updated accordingly

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

5.3.35. Trifluridine, tipiracil - LONSURF (CAP) - EMEA/H/C/003897/II/0002/G

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations to: 1) update of sections 4.2, 4.4 and 5.2 of the SmPC following availability of the final clinical study report for study TO-TAS-102-106: a phase I, open-label study evaluating the safety, tolerability, and pharmacokinetics of TAS-102 in patients with advanced solid tumours and varying degrees of hepatic impairment (requested in MEA 002). The RMP (version 5.0) is updated accordingly to remove the missing information 'use in patients with moderate to severe hepatic impairment' and to add 'hyperbilirubinaemia in patients with baseline moderate to severe hepatic impairment' as important potential risk; 2) update of sections 4.5 and 5.2 of the SmPC following availability of the results in vitro CYP induction study of tipiracil hydrochloride (TPI) using the appropriate concentration of TPI (requested in a recommendation). The RMP is updated accordingly; 3) update of section 4.2 of the SmPC in order to correct inconsistencies in the dose calculation according to body surface area. The package leaflet is updated to add 'interstitial lung disease'. Finally, the MAH took the opportunity to update Annex IIIA in accordance with the latest QRD template

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. Agalsidase beta - FABRAZYME (CAP) - PSUSA/00000070/201607

Applicant: Genzyme Europe BV

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Asenapine - SYCREST (CAP) - PSUSA/00000256/201608

Applicant: N.V. Organon

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Brimonidine[4] - MIRVASO (CAP) - PSUSA/00010093/201608 (with RMP)

Applicant: Galderma International

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Ceftazidime, avibactam - ZAVICEFTA (CAP) - PSUSA/00010513/201608

Applicant: AstraZeneca AB

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Cobicistat - TYBOST (CAP) - PSUSA/00010081/201608

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Cobicistat, elvitegravir, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - PSUSA/00010082/201608

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[4] Centrally authorised product only

6.1.7. Cobimetinib - COTELLIC (CAP) - PSUSA/00010450/201608 (with RMP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Collagenase clostridium histolyticum[5] - XIAPEX (CAP) - PSUSA/00000871/201608

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Copper (^{64}Cu) chloride - CUPRYMINA (CAP) - PSUSA/00010040/201608

Applicant: Sparkle S.r.l.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Crizotinib - XALKORI (CAP) - PSUSA/00010042/201608

Applicant: Pfizer Limited

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Dabrafenib - TAFINLAR (CAP) - PSUSA/00010084/201608

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Deferiprone - FERRIPROX (CAP) - PSUSA/00000940/201608 (with RMP)

Applicant: Apotex Europe BV

PRAC Rapporteur: Caroline Laborde

[5] Indicated in the treatment of Dupuytren's contracture and treatment of Peyronie's disease only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Desloratadine, pseudoephedrine - AERINAZE (CAP) - PSUSA/00000963/201607

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Dinutuximab - UNITUXIN (CAP) - PSUSA/00010420/201608

Applicant: United Therapeutics Europe Ltd

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated), haemophilus type b conjugate vaccine (adsorbed) - VAXELIS (CAP) - PSUSA/00010469/201608

Applicant: MCM Vaccine B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Dronedarone - MULTAQ (CAP) - PSUSA/00001180/201607

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Eliglustat - CERDELGA (CAP) - PSUSA/00010351/201608

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Elosulfase alfa - VIMIZIM (CAP) - PSUSA/00010218/201608

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Elvitegravir - VITEKTA (CAP) - PSUSA/00002577/201608

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Emtricitabine, rilpivirine, tenofovir alafenamide - ODEFSEY (CAP) - PSUSA/00010514/201608 (with RMP)

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Emtricitabine, rilpivirine, tenofovir disoproxil - EVIPLERA (CAP) - PSUSA/00009142/201608

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Enzalutamide - XTANDI (CAP) - PSUSA/00010095/201608

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/201608

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.24. Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/201608

Applicant: Shield TX (UK) Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Florbetaben (^{18}F) - NEURACEQ (CAP) - PSUSA/00010094/201608

Applicant: Piramal Imaging Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Pioglitazone - ACTOS (CAP), GLUSTIN (CAP); pioglitazone, glimepiride - TANDEMACT (CAP); pioglitazone, metformin - COMPETACT (CAP), GLUBRAVA (CAP); PSUSA/00002417/201607

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Human alpha$_1$-proteinase inhibitor - RESPREEZA (CAP) - PSUSA/00010410/201608

Applicant: CSL Behring GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Human coagulation factor VIII, human von Willebrand factor[6] - VONCENTO (CAP) - PSUSA/00010102/201608

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[6] Centrally authorised product only

6.1.29. Lenvatinib - KISPLYX (CAP), LENVIMA (CAP) - PSUSA/00010380/201608 (with RMP)

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Linaclotide - CONSTELLA (CAP) - PSUSA/00010025/201608 (with RMP)

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Loxapine[7] - ADASUVE (CAP) - PSUSA/00010113/201608 (with RMP)

Applicant: Ferrer Internacional S.A.

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Mecasermin - INCRELEX (CAP) - PSUSA/00001942/201608 (with RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Natalizumab - TYSABRI (CAP) - PSUSA/00002127/201608

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Nonacog alfa - BENEFIX (CAP) - PSUSA/00002183/201608

Applicant: Pfizer Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

[7] As pre-dispensed inhalation powder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Ospemifene - SENSHIO (CAP) - PSUSA/00010340/201608

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Pandemic influenza vaccine (H5N1) (whole virion, vero cell derived, inactivated) - PANDEMIC INFLUENZA VACCINE H5N1 BAXTER (CAP); prepandemic influenza vaccine (H5N1) (whole virion, vero cell derived, inactivated) - VEPACEL (CAP) - PSUSA/00002282/201608

Applicant: Nanotherapeutics Bohumil Sro

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Panobinostat - FARYDAK (CAP) - PSUSA/00010409/201608 (with RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Peginterferon alpha-2b - PEGINTRON (CAP); VIRAFERONPEG (CAP) - PSUSA/00002327/201607 (with RMP)

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Pomalidomide - IMNOVID (CAP) - PSUSA/00010127/201608

Applicant: Celgene Europe Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Safinamide - XADAGO (CAP) - PSUSA/00010356/201608

Applicant: Zambon SpA

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Sebelipase alfa - KANUMA (CAP) - PSUSA/00010422/201608

Applicant: Alexion Europe SAS

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Teduglutide - REVESTIVE (CAP) - PSUSA/00009305/201608

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Vemurafenib - ZELBORAF (CAP) - PSUSA/00009329/201608

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Vernakalant hydrochloride - BRINAVESS (CAP) - PSUSA/00003109/201608

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

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. Amlodipine, valsartan - COPALIA (CAP), DAFIRO (CAP), EXFORGE (CAP), IMPRIDA (CAP); amlodipine, hydrochlorothiazide, valsartan - COPALIA HCT (CAP), DAFIRO HCT (CAP), EXFORGE HCT (CAP); NAP - PSUSA/00010344/201606

Applicant(s): Novartis Europharm Ltd (Copalia, Copalia HCT, Dafiro, Dafiro HCT, Exforge, Exforge HCT, Imprida), various

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Busulfan - BUSILVEX (CAP); NAP - PSUSA/00000464/201607

Applicant(s): Pierre Fabre Medicament (Busilvex), various

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Desloratadine - AERIUS (CAP); AZOMYR (CAP); DASSELTA (CAP); DESLORATADINE ACTAVIS (CAP); DESLORATADINE RATIOPHARM (CAP); DESLORATADINE TEVA (CAP); NEOCLARITYN (CAP); NAP - PSUSA/00000962/201607

Applicant(s): Merck Sharp & Dohme Limited (Aerius, Azomyr, Neoclarityn), Krka, d.d., Novo mesto (Dasselta), Actavis Group PTC ehf (Desloratadine Actavis), Ratiopharm GmbH (Desloratadine Ratiopharm), Teva B.V. (Desloratadine Teva), various

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Human coagulation factor IX - NONAFACT (CAP); NAP - PSUSA/00001617/201607

Applicant(s): Sanquin Plasma Products B.V. (Nonafact), various

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Human protein C - CEPROTIN (CAP); NAP - PSUSA/00002563/201607

Applicant(s): Baxter AG (Ceprotin), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Palonosetron - ALOXI (CAP); NAP - PSUSA/00002268/201607

Applicant(s): Helsinn Birex Pharmaceuticals Ltd (Aloxi), various

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Beclometasone, formoterol[8] (NAP) - PSUSA/00010068/201607

Applicant: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Desogestrel (NAP) - PSUSA/00000966/201607

Applicant: various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Fluticasone propionate, formoterol fumarate dihydrate (NAP)– PSUSA/00010339/201607

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide (NAP) - PSUSA/00010390/201607

Applicant: various

PRAC Lead: Doris Stenver

[8] Inhalative application

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Lovastatin (NAP) - PSUSA/00010051/201607

Applicant: various

PRAC Lead: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Lubiprostone (NAP) - PSUSA/00010290/201607

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Magnesium sulphate, sodium sulphate, potassium sulphate (NAP) - PSUSA/00010239/201608

Applicant: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Mitoxantrone (NAP) - PSUSA/00002076/201606

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Pilocarpinel, timolol (NAP) - PSUSA/00002408/201607

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Poliovirus type 1, poliovirus type 2, poliovirus type 3 vaccine (oral, live, attenuated) (NAP) - PSUSA/00002458/201607

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Ropinirole (NAP) - PSUSA/00002661/201607

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Tamsulosin (NAP) - PSUSA/00002847/201607

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Trimetazidine (NAP) - PSUSA/00003043/201608

Applicant: various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Meloxicam (NAP) - PSUSA/00010474/201607

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Phleum pratense[9] (NAP) - PSUSA/00010475/201607

Applicant: various

PRAC Lead: Qun-Ying Yue

[9] Allergen for therapy, oromucosal use, authorised via mutually recognition procedure

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/LEG 168

Applicant: Pfizer Limited

PRAC Rapporteur: Patrick Batty

Scope: Submission of a review on the apparent increase in reports of adverse events (AEs) linked to elevated liver function tests (LFT) and the possible need for additional risk minimisation measures. The review also includes an analysis of underlying reasons for the change in frequency of the LFT abnormalities from the time of granting of the marketing authorisation (MA) to any other adverse drug reactions currently listed in section 4.8 of the SmPC and details on the results of the statistical analysis of studies from registers such as the British Society for Rheumatology Biologicals Register (BSRBR), German register for the long-term observation of therapy with biologics in adult patients with rheumatoid arthritis (RABBIT), as requested in the conclusions of EMEA/H/C/PSUSA/00001295/201602 adopted by PRAC in September 2016

Action: For adoption of advice to CHMP

6.4.2. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/LEG 034

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Submission of a cumulative review of data from all sources on the risk of rebound multiple sclerosis (MS) with fingolimod, as requested in the conclusions of EMEA/H/C/PSUSA/00001393/201602 adopted by PRAC in October 2016

Action: For adoption of advice to CHMP

6.4.3. Levetiracetam - KEPPRA (CAP) - EMEA/H/C/000277/LEG 084

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Submission of a cumulative review on the teratogenic risk and the risk of neurodevelopmental disorders associated with the use of levetiracetam during pregnancy, based on data from all available sources as requested in the conclusions of EMEA/H/C/PSUSA/00001846/201511 adopted by PRAC in September 2016

Action: For adoption of advice to CHMP

6.4.4. Oseltamivir - TAMIFLU (CAP) - EMEA/H/C/000402/LEG 104

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of a cumulative summary table of serious adverse events (SAEs) from clinical trials as requested in the conclusions of EMEA/H/C/PSUSA/00002225/201509 adopted by PRAC in May 2016

Action: For adoption of advice to CHMP

6.4.5. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[10]) - EMEA/H/W/002300/LEG 013

Applicant: GSK Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of further information on studies Malaria-055 (an efficacy study of GSK Biologicals' candidate malaria vaccine 257049 against malaria disease in infants and children in Africa) and Malaria-076 (an extension to study Malaria-055 PRI to evaluate the long-term efficacy, safety and immunogenicity of GSK Biologicals' candidate malaria vaccine in infants and children in Africa), as well as on the ad-hoc analysis of mortality by gender, on the post-hoc analysis of cerebral malaria and regarding the risk-benefit analysis, as requested in the conclusions of EMEA/H/W/002300/PSUV/011 adopted by PRAC in November 2016

Action: For adoption of advice to CHMP

6.4.6. Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/LEG 052

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Submission of an analysis of data collected through a follow-up questionnaire as a routine pharmacovigilance activity regarding spontaneous reports on abuse, misuse, dependence and withdrawal symptoms including a discussion on the potential added value of the collected data. In addition, the MAH submitted a detailed analysis of cases of 'hepatobiliary disorders' as requested in the conclusions of PSUSA/00002511/201601 adopted by PRAC in September 2016

Action: For adoption of advice to CHMP

6.4.7. Pregabalin - PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/LEG 005

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Submission of an analysis of data collected through a follow-up questionnaire as a routine pharmacovigilance activity regarding spontaneous reports on abuse, misuse, dependence and withdrawal symptoms including a discussion on the potential added value of the collected data. In addition, the MAH submitted a detailed analysis of cases of 'hepatobiliary disorders' as requested in the conclusions of PSUSA/00002511/201601

[10] 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)

adopted by PRAC in September 2016

Action: For adoption of advice to CHMP

6.4.8. Vardenafil - LEVITRA (CAP) - EMEA/H/C/000475/LEG 026

Applicant: Bayer Pharma AG

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a cumulative review and a discussion on cerebrovascular disorders with data from all available sources (clinical trials, post-marketing experience, literature) including information regarding time to onset, age of patients, dose of vardenafil, confounding or risk factors as well as any information on dechallenge/rechallenge as requested in the conclusions of PSUSA/00003098/201603 adopted by PRAC in November 2016

Action: For adoption of advice to CHMP

6.4.9. Vardenafil - VIVANZA (CAP) - EMEA/H/C/000488/LEG 026

Applicant: Bayer Pharma AG

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a cumulative review and a discussion on cerebrovascular disorders with data from all available sources (clinical trials, post-marketing experience, literature) including information regarding time to onset, age of patients, dose of vardenafil, confounding or risk factors as well as any information on dechallenge/rechallenge as requested in the conclusions of PSUSA/00003098/201603 adopted by PRAC in November 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)[11]

7.1.1. Iron intravenous (IV) (NAP) - EMEA/H/N/PSP/J/0053

Applicant: Mesama Consulting

PRAC Rapporteur: Claire Ferard

Scope: PASS protocol for a study evaluating the risk of severe hypersensitivity reactions and assessing the risk of anaphylactic or severe immediate hypersensitivity reactions on the day of or the day after first IV iron use

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

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

7.1.2. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/PSA/S/0016

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: Updated PASS protocol (version 2.0) for study CC-5013-MDS-012: a prospective non-interventional PASS designed as myelodysplastic syndromes (MDS) disease registry of patients with transfusion dependent international prognostic scoring system (IPSS) low or intermediate-1-risk MDS and isolated del(5q) (from II/56 (extension of indication))

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

7.1.3. Valproate (NAP) - EMEA/H/N/PSA/J/0015

Applicant: Sanofi

PRAC Rapporteur: Sabine Straus

Scope: Updated protocol for a joint drug utilisation study (DUS) using EU databases to study the effectiveness of the imposed risk minimisation measures following the conclusion of the referral procedure under Article 31 of Directive 2001/83/EC completed in 2014 (EMEA/H/A-31/1387) and to further characterise the prescribing patterns for valproate

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[12]

7.2.1. Eluxadoline - TRUBERZI (CAP) - EMEA/H/C/004098/MEA 005

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: PASS protocol for study EVM-19596-00-001: a drug utilisation study (DUS) (RMP category 3) using relevant health care databases at two different time periods in order to define the compliance to contraindications over time and the number of subjects diagnosed with pancreatitis after eluxadoline treatment (as requested in the initial MAA opinion)

Action: For adoption of advice to CHMP

7.2.2. Fenofibrate, simvastatin - CHOLIB (CAP) - EMEA/H/C/002559/MEA 002.5

Applicant: Mylan Products Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 002.4: submission of a revised protocol in addition to the third status report 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 September 2016. Submission of a revised protocol and questionnaire for the

[12] 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

questionnaire-based study EUPAS15741: assessment of prescribing conditions of Cholib: a European study in Austria, Croatia, Czech Republic, Portugal, Slovakia and Slovenia, as per the request for supplementary information (RSI) adopted in October 2016

Action: For adoption of advice to CHMP

7.2.3. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/MEA 015

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Patrick Batty

Scope: PASS protocol for study GS-EU-313-4172: a non-interventional study to assess the safety profile of idelalisib in patients with refractory follicular lymphoma (FL)

Action: For adoption of advice to CHMP

7.2.4. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/MEA 016

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Patrick Batty

Scope: PASS protocol for study GS-EU-313-4226: a cross-sectional PASS to assess healthcare provider awareness of risks associated with Zydelig in the European Union

Action: For adoption of advice to CHMP

7.2.5. Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/MEA 001.3

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's responses to MEA 001.1 and MEA 001.2 on PASS protocol for study 178-CL-114: 'evaluation of cardiovascular events in users of mirabegron and other treatments for overactive bladder: on cardiovascular events' as adopted in October 2013 and July 2016 respectively

Action: For adoption of advice to CHMP

7.2.6. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 008

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Almath Spooner

Scope: Protocol for study D3820R00008: a US post-marketing, comparative, observational study to evaluate the cardiovascular safety of naloxegol in patients with non-cancer pain in comparison to other treatments for opioid induced constipation

Action: For adoption of advice to CHMP

7.2.7. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 002.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 002.1: PASS protocol for study CLCZ696B2014: a non-interventional post-authorisation European database safety study (RMP category 3) to characterize the risk of angioedema and other specific safety events of interest in association with use of Entresto (sacubitril/valsartan) in adult patients with heart failure, as per request for supplementary information (RSI) adopted in November 2016

Action: For adoption of advice to CHMP

7.2.8. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 004.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA/004.1: PASS protocol for study CLCZ696B2015: a non-interventional post-authorisation European database safety study (category 3) to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of sacubitril/valsartan, as per request for supplementary information (RSI) adopted in November 2016

Action: For adoption of advice to CHMP

7.2.9. Zonisamide - ZONEGRAN (CAP) - EMEA/H/C/000577/MEA 038

Applicant: Eisai Ltd

PRAC Rapporteur: Almath Spooner

Scope: PASS protocol for study E2090-E044-501: a non-interventional PASS: a retrospective database study of the prescribing of zonisamide in UK general practice: a drug utilisation study (DUS) as part of post marketing safety surveillance (from II/65)

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[13]

7.3.1. Flupirtine maleate - EMEA/H/N/PSR/J/0007

Applicant(s): Meda Pharma GmbH & Co KG (Flupigil); Meda Pharma - Produtos Farmaceuticos, S.A. (Metanor)

PRAC Rapporteur: Valerie Strassmann

Scope: Submission of the final study results for an imposed non-interventional PASS: retrospective chart review to evaluate the effectiveness of the risk minimization measures for the use of flupirtine 100 mg immediate-release capsules in daily practice

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

Action: For adoption of recommendation to CMDh

7.4. Results of PASS non-imposed in the marketing authorisation(s)[14]

7.4.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/II/0108/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations including 1) submission of the final clinical study report from epidemiological IM101045A study: safety of non-biologic disease-modifying antirheumatic drugs (DMARDs) and biologic treatment for rheumatoid arthritis (RMP category 3 study); 2) submission of the final clinical study report from epidemiological IM101045B study: safety and outcomes in patients treated with abatacept and other anti-rheumatic therapies (RMP category 3 study). IM101045A and IM101045B are both observational studies, sharing overlapping safety objectives (assessment of the risk of infections, infusion-related reactions, autoimmune disorders, injection reactions and combination use)

Action: For adoption of PRAC Assessment Report

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

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of PRAC Assessment Report

7.4.3. Buprenorphine, naloxone - SUBOXONE (CAP) - EMEA/H/C/000697/II/0035

Applicant: Indivior UK Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final study report for PEUS004: a retrospective observational survey on Suboxone use in France. The RMP (version 12.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/II/0100

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of the final report for study 1160.144 evaluating the potential off-label

[14] 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

use of dabigatran etexilate in Europe: a drug utilisation study (DUS) in Cegedim France, Denmark, and Clinical Practice Research Datalink (CPRD) UK

Action: For adoption of PRAC Assessment Report

7.4.5. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/II/0101

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of the final report for study 1160.162: an observational study assessing the management of gastrointestinal and urogenital bleeding events in patients with non valvular atrial fibrillation treated with dabigatran etexilate

Action: For adoption of PRAC Assessment Report

7.4.6. Dexamethasone - OZURDEX (CAP) - EMEA/H/C/001140/II/0025

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report for PASS 206207-025: a prospective observational study to evaluate the long-term safety in real-world clinical practice

Action: For adoption of PRAC Assessment Report

7.4.7. Human rotavirus, live attenuated - ROTARIX (CAP) - EMEA/H/C/000639/II/0094

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final study report for EPI-ROTA-007 VS US DB: a phase IV, open, observational study of the safety of Rotarix, administered to a birth cohort in US States health insurance plans. The RMP (version 17) is updated in order to amend information in relation to EPI-ROTA-007 VS US DB study, EPI-ROTA-052 BOD EU SUPP (an observational community-based strain surveillance study) as agreed in the conclusions of variation II/86. In addition, the MAH took this opportunity to further update the RMP with the new due date for submission of the final study report for ROTA-085 PMS (a special drug use investigation for Rotarix (investigation of incidence of intussusception after vaccination for rotavirus gastroenteritis) conducted with the objective to determine the incidence of intussusception after vaccination with Rotarix in Japan)

Action: For adoption of PRAC Assessment Report

7.4.8. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/II/0064

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final study report for study MI-MA194: a post-marketing

observational evaluation of the safety of Fluenz in children and adolescents with high-risk conditions

Action: For adoption of PRAC Assessment Report

7.4.9. Levodopa, carbidopa, entacapone - CORBILTA (CAP) - EMEA/H/C/002785/II/0009

Applicant: Orion Corporation

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of the final report of pharmacoepidemiological registry study CCOM998A2001 (RMP category 3) evaluating the risk of incident myocardial infarction in Parkinson's disease patients with add-on entacapone to levodopa/dopa-decarboxylase inhibitor (DDCI) compared to other add-on Parkinson's disease therapy without entacapone - a retrospective cohort study using data from MarketScan, as requested by PRAC in the conclusions of EMEA/H/C/PSUSA/00000547/201510 in May 2016. The RMP (version 2.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.10. Levodopa, carbidopa, entacapone - CORBILTA (CAP) - EMEA/H/C/002785/II/0010

Applicant: Orion Corporation

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of the final report of pharmacoepidemiological registry study ER11-9411 (RMP category 3) evaluating the risk of developing prostate cancer in entacapone and levodopa/dopa-decarboxylase inhibitor (DDCI) users compared to levodopa/DDCI users without entacapone - a nation-wide retrospective register-based study, as requested by PRAC in the conclusions of EMEA/H/C/PSUSA/00000547/201510 in May 2016. The RMP (version 2.0) is updated accordingly

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. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 053.3

Applicant: Genzyme Europe BV

PRAC Rapporteur: Claire Ferard

Scope: Epidemiology PASS study report for study ALGMYC07390 evaluating the prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions

Action: For adoption of advice to CHMP

7.5.2. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 005

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First and second interim reports for study MB102134, a drug utilisation study (DUS): observational single-cohort data base study with descriptive data analyses among patients receiving dapagliflozin within electronic medical records (EMRs) in Europe. This study aims at describing the utilisation patterns of dapagliflozin during the first 3.5 years after marketing authorisation and launch in Europe and the characteristics of European patients prescribed dapagliflozin by age, sex, dapagliflozin dose, country, selected comorbidities, and selected concomitant medications

Action: For adoption of advice to CHMP

7.5.3. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/MEA 008.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First and second interim reports for study MB102134, a drug utilisation study (DUS): observational single-cohort data base study with descriptive data analyses among patients receiving dapagliflozin within electronic medical records (EMRs) in Europe. This study aims at describing the utilisation patterns of dapagliflozin during the first 3.5 years after marketing authorisation and launch in Europe and the characteristics of European patients prescribed dapagliflozin by age, sex, dapagliflozin dose, country, selected comorbidities, and selected concomitant medications

Action: For adoption of advice to CHMP

7.5.4. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/MEA 004

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First and second interim reports for study MB102134, a drug utilisation study (DUS): observational single-cohort data base study with descriptive data analyses among patients receiving dapagliflozin within electronic medical records (EMRs) in Europe. This study aims at describing the utilisation patterns of dapagliflozin during the first 3.5 years after marketing authorisation and launch in Europe and the characteristics of European patients prescribed dapagliflozin by age, sex, dapagliflozin dose, country, selected comorbidities, and selected concomitant medications

Action: For adoption of advice to CHMP

7.5.5. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 007

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First and second interim reports for study MB102134, a drug utilisation study (DUS):

observational single-cohort data base study with descriptive data analyses among patients receiving dapagliflozin within electronic medical records (EMRs) in Europe. This study aims at describing the utilisation patterns of dapagliflozin during the first 3.5 years after marketing authorisation and launch in Europe and the characteristics of European patients prescribed dapagliflozin by age, sex, dapagliflozin dose, country, selected comorbidities, and selected concomitant medications

Action: For adoption of advice to CHMP

7.5.6. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/ANX 038.7

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Third annual interim report for study CICL670E2422: an observational, multicentre study to evaluate the safety of deferasirox in the treatment of paediatric patients with non-transfusion-dependent iron overload

Action: For adoption of advice to CHMP

7.5.7. Efavirenz, emtricitabine , tenofovir disoproxil - ATRIPLA (CAP) - EMEA/H/C/000797/MEA 039.5

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd.

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 039.4: third annual report for malignant events associated with efavirenz: Diagnostic Consulting Network (DCN) report as a routine risk minimisation measures, as adopted by PRAC in November 2016

Action: For adoption of advice to CHMP

7.5.8. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 027.4

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: First progress report of the ENEIDA registry: a long-term, non-interventional observational study of patients with inflammatory bowel disease (IBD) in Spain to evaluate whether the use of golimumab is associated with a risk of colectomy for intractable disease, advanced neoplasia (colorectal cancer or high grade dysplasia), and hepatosplenic T-cell lymphoma (HSTCL) in patients with ulcerative colitis (UC) as compared with alternative therapies for similar severity of disease

Action: For adoption of advice to CHMP

7.5.9. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/ANX 191.5

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Eva Segovia

Scope: Third progress report for study CSTI571I2201: a European observational registry collecting efficacy and safety data in newly diagnosed paediatric Philadelphia positive (Ph+) acute lymphoblastic leukaemia (ALL) patients treated with chemotherapy + imatinib ± hematopoietic stem cell treatment (±HSCT)

Action: For adoption of advice to CHMP

7.5.10. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/MEA 133.11

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Ninth annual paediatric inflammatory bowel disease (IBD) registry (DEVELOP) report on long-term safety and efficacy of infliximab and other therapies, safety and efficacy of variable infliximab dosing intervals, episodic therapy, monotherapy (initiated de novo or following discontinuation of concomitant immunomodulators), combined infliximab and immunomodulator therapy (azathioprine/6-mercaptopurine (AZA/6-MP) or methotrexate (MTX))

Action: For adoption of advice to CHMP

7.5.11. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/ANX 001.4

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Fourth interim study results of a five-year long-term observational study with ivacaftor in patients with cystic fibrosis (CF), including also microbiological and clinical endpoints

Action: For adoption of advice to CHMP

7.5.12. Mannitol - BRONCHITOL (CAP) - EMEA/H/C/001252/ANX 002.9

Applicant: Pharmaxis Pharmaceuticals Limited

PRAC Rapporteur: Julie Williams

Scope: Seventh interim analysis of the cystic fibrosis (CF) study, which aims to compare the rate of identified and potential risks for Bronchitol in CF between Bronchitol-exposed patients and an unexposed patient group matched (via propensity score modelling) for age, disease severity (FEV1 % predicted), concomitant medications and presence of chronic *Pseudomonas*

Action: For adoption of advice to CHMP

7.5.13. Nalmefene - SELINCRO (CAP) - EMEA/H/C/002583/MEA 001.2

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Martin Huber

Scope: Interim study report for PASS 14910A (EUPAS5678): a non-interventional multi-

country prospective cohort study investigating patterns of use of Selincro and frequency of adverse drug reactions in routine clinical practice

Action: For adoption of advice to CHMP

7.5.14. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 009

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Almath Spooner

Scope: Annual progress study report for study D3820R00008: a US post-marketing, comparative, observational study to evaluate the cardiovascular safety of naloxegol in patients with non-cancer pain in comparison to other treatments for opioid induced constipation

Action: For adoption of advice to CHMP

7.5.15. Oseltamivir - TAMIFLU (CAP) - EMEA/H/C/000402/LEG 087.4

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Fourth annual review on pregnancy cases

Action: For adoption of advice to CHMP

7.5.16. Oseltamivir - TAMIFLU (CAP) - EMEA/H/C/000402/MEA 099.1

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Interim study report for study BV29684: a non-interventional cohort study assessing the safety of oseltamivir exposure in pregnant women

Action: For adoption of advice to CHMP

7.5.17. Perampanel - FYCOMPA (CAP) - EMEA/H/C/002434/MEA 004.5

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Julie Williams

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

Action: For adoption of advice to CHMP

7.5.18. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/MEA 256.9

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Caroline Laborde

Scope: Second interim study report for a drug utilisation study (DUS) GS-EU-104-0433 in paediatric patients with human immunodeficiency virus (HIV)-1 infection, to describe the characteristics of HIV-1 infected patients up to 18 years of age treated with Viread within the EU in order to determine if they are being managed in accordance with the European SmPC. In addition, MAH's responses to the request for supplementary information (RSI) as adopted by PRAC in March 2016 for MEA 0256.6 on the first interim study report

Action: For adoption of advice to CHMP

7.5.19. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/MEA 273.2

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Caroline Laborde

Scope: Six-monthly interim results including a status report regarding the inclusion of patients and the matching process within the planned cohort 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

7.6. Others

7.6.1. Bazedoxifene - CONBRIZA (CAP) - EMEA/H/C/000913/MEA 012.8

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Statistical analysis plan of the ongoing EU B1781044 PASS for bazedoxifene: a cohort study of venous thromboembolism and other clinical endpoints among osteoporotic women prescribed bazedoxifene, bisphosphonates or raloxifene in Europe) for the period from October 2015 to October 2016, as per the request for supplementary information (RSI) adopted in July 2016

Action: For adoption of advice to CHMP

7.6.2. Desloratadine - AERIUS (CAP) - EMEA/H/C/000313/MEA 065.2; AZOMYR (CAP) - EMEA/H/C/000310/MEA 065.2; NEOCLARITYN (CAP) - EMEA/H/C/000314/MEA 065.2

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: Statistical analysis plan for a Nordic register-based study exploring the association between the use of desloratadine and risk of seizures, supraventricular tachycardia, and atrial fibrillation or flutter (from WS/0641, CHMP adoption dated 26 March 2015)

Action: For adoption of advice to CHMP

7.6.3. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 064

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Feasibility study for an observational cohort study (RMP category 3) utilising the Tysabri outreach: unified commitment to health (TOUCH) prescribing programme (5 year enrolment: January 2016-December 2020 + 3 year follow up) including a feasibility assessment for inclusion of EU registry data to estimate the risk of progressive multifocal leukoencephalopathy (PML) among patients on Tysabri switching from the newer disease-modifying therapies (DMTs) and from established DMTs

Action: For adoption of advice to CHMP

7.6.4. Oseltamivir - TAMIFLU (CAP) - EMEA/H/C/000402/MEA 102.2

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Annual report for study NV20234: a double-blind, randomized, stratified multicentre trial evaluating conventional and double dose oseltamivir in the treatment of immunocompromised patients with influenza exploring the safety and efficacy of oseltamivir in immunocompromised patients

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. Anagrelide - XAGRID (CAP) - EMEA/H/C/000480/S/0077 (without RMP)

Applicant: Shire Pharmaceutical Contracts Ltd.

PRAC Rapporteur: Claire Ferard

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Cholic acid - KOLBAM (CAP) - EMEA/H/C/002081/S/0020 (without RMP)

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Patrick Batty

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Histamine dihydrochloride - CEPLENE (CAP) - EMEA/H/C/000796/S/0030 (without RMP)

Applicant: Meda AB

PRAC Rapporteur: Almath Spooner

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0005 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.5. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/S/0036 (with RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Claire Ferard

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.6. Tocofersolan - VEDROP (CAP) - EMEA/H/C/000920/S/0019 (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

8.2.1. Fampridine - FAMPYRA (CAP) - EMEA/H/C/002097/R/0037 (without RMP)

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Sabine Straus

Scope: 1-year conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Aliskiren - RASILEZ (CAP) - EMEA/H/C/002406/R/0021 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Axitinib - INLYTA (CAP) - EMEA/H/C/002406/R/0021 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Helga Haugom Olsen

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Catridecacog - NOVOTHIRTEEN (CAP) - EMEA/H/C/002284/R/0020 (without RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Claire Ferard

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Copper (^{64}Cu) chloride - CUPRYMINA (CAP) - EMEA/H/C/002136/R/0014 (with RMP)

Applicant: Sparkle S.r.l.

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Decitabine - DACOGEN (CAP) - EMEA/H/C/002221/R/0030 (without RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Claire Ferard

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Glycopyrronium bromide - SEEBRI BREEZHALER (CAP) - EMEA/H/C/002430/R/0020 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Glycopyrronium bromide - TOVANOR BREEZHALER (CAP) - EMEA/H/C/002690/R/0022 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Glycopyrronium bromide - ENUREV BREEZHALER (CAP) - EMEA/H/C/002691/R/0020 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/R/0038 (without RMP)

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Temsirolimus - TORISEL (CAP) - EMEA/H/C/000799/R/0065 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Zoledronic acid - ZOLEDRONIC ACID MYLAN (CAP) - EMEA/H/C/002482/R/0013 (with RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Doris Stenver

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Zoledronic acid - ZOLEDRONIC ACID TEVA (CAP) - EMEA/H/C/002439/R/0018 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Zoledronic acid - ZOLEDRONIC ACID TEVA PHARMA (CAP) - EMEA/H/C/002437/R/0014 (without RMP)

Applicant: Teva B.V.

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. Canagliflozin – INVOKANA (CAP) - EMEA/H/C/002649/II/0026; canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0023

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: PRAC consultation on type II variations to update of section 4.4 of the SmPC in order to update the safety information: the term 'and fatal' is added when describing the diabetic ketoacidosis (DKA) cases that have been reported. The Package Leaflet is updated accordingly: term 'rare but serious, sometimes life-threatening and fatal' is added when describing DKA. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

10.3.1. Brodalumab – EMEA/H/C/003959

Scope: PRAC consultation on an initial application for Kyntheum (brodalumab) with a proposed indication for the treatment of moderate to severe plaque psoriasis

Action: For adoption of advice to CHMP

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

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

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. EMA reflection paper on extrapolation across age groups - update

PRAC lead: Jolanta Gulbinovič

Action: For discussion

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

Action: For discussion

12.5. Cooperation with International Regulators

12.5.1. Gaucher disease - a strategic collaborative approach between EMA and FDA

Action: For discussion

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan for 2017

Action: For adoption

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Good Pharmacovigilance Practices (GVP) module II on 'Pharmacovigilance system master file' – Revision 2

Action: For adoption

12.9.2. Pharmacovigilance systems and their quality systems

None

12.9.3. Pharmacovigilance inspections

None

12.9.4. Pharmacovigilance audits

None

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

12.10.1. PSUR single assessment (PSUSA) for CAPs only - editorial changes to product information

Action: For discussion

12.10.2. Roadmap for PSUR issues - explanatory note to Good Pharmacovigilance Practice (GVP) module VII on 'Periodic safety update report' and 'Questions & Answers (Q&A)' document to assessors

PRAC lead: Menno Van Der Elst

Action: For discussion

12.10.3. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.4. PSURs repository

None

12.10.5. 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- EudraVigilance auditable requirement project update

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Good Pharmacovigilance Practice (GVP) module V on 'Risk management systems' - finalisation

Action: For adoption

12.14.2. Good Pharmacovigilance Practice (GVP) module V on 'Risk management systems' - outcome of PRAC survey

PRAC lead: Sabine Straus

Action: For discussion

12.14.3. Risk management plan (RMP) template for industry - finalisation

Action: For adoption

12.14.4. Risk management plan (RMP) review process - review of experience with the revised process and quantitative survey results

Action: For discussion

12.14.5. Risk management systems

None

12.14.6. 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. Good Pharmacovigilance Practices (GVP) – PRAC review and adoption of revised GVP modules in 2017: update on GVP status and overview

Action: For discussion

12.20.2. Industry stakeholder platform on the operation of the EU pharmacovigilance – Feedback from the tenth industry stakeholder platform meeting held on 3 February 2017

Action: For discussion

12.20.3. Strategy on measuring the impact of pharmacovigilance activities – report from the workshop held on 5-6 December 2016

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/