3 July 2017
EMA/PRAC/423016/2017

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 3-6 July 2017

Chair: June Raine – Vice-Chair: Almath Spooner

3 July 2017, 13:00 – 19:30, room 3/A

4 July 2017, 08:30 – 19:30, room 3/A

5 July 2017, 08:30 – 19:30, room 3/A

6 July 2017, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

20 July 2017, 09:00 – 12:00, room 7/B, via adobe connect

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 3-6 July 2017. See July 2017 PRAC minutes (to be published post September 2017 PRAC meeting).

1.2. Agenda of the meeting on 3-6 July 2017

Action: For adoption

1.3. Minutes of the previous meeting on 6-9 June 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

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. Daclizumab - ZINBRYTA (CAP) – EMEA/H/A-20/1456

Applicant(s): Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia; PRAC Co-rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Review of the benefit-risk balance following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004 based on pharmacovigilance data

Action: For discussion or adoption of PRAC recommendation on provisional measures

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

Applicant(s): 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)

3.2.3. Valproate and related substances: sodium valproate, valproic acid, valproate semisodium, valpromide (NAP) - EMEA/H/A-31/1454

Applicant(s): Sanofi-Aventis, various

PRAC Rapporteur: Sabine Straus; PRAC Co-rapporteur: Jean-Michel Dogné

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 for the public hearing and stakeholders meeting

3.3. Procedures for finalisation

3.3.1. Lactose of bovine origin-containing medicinal products[2]: methylprednisolone (NAP) - EMEA/H/A-31/1449

Applicant(s): 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

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

Action: For adoption of a recommendation to CMDh

3.4. Re-examination procedures[3]

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

Applicant(s): Mallinckrodt Deutschland GmbH (Optimark); various

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Valerie Strassmann

Scope: Re-examination procedure under Article 32 of Directive 2001/83/EC of the review of the benefit-risk balance of GdCA 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

3.5. Others

None

4. Signals assessment and prioritisation[4]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Ritonavir - NORVIR (CAP); lopinavir, ritonavir – KALETRA (CAP); levothyroxine (NAP)

Applicant(s): AbbVie Ltd. (Kaletra, Norvir), various

PRAC Rapporteur: To be appointed

Scope: Signal of interaction possibly leading to decreased levothyroxine efficacy and hypothyroidism

Action: For adoption of PRAC recommendation

EPITT 18896 – New signal

Lead Member State(s): FR, NL

4.1.2. Tofacitinib – XELJANZ (CAP)

Applicant(s): Pfizer Limited

[3] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[4] 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: Sabine Straus

Scope: Signal of angioedema

Action: For adoption of PRAC recommendation

EPITT 18904 – New signal

Lead Member State(s): NL

4.2. New signals detected from other sources

4.2.1. Desloratadine – AERINAZE (CAP), AERIUS (CAP), AZOMYR (CAP), DASSELTA (CAP), DESLORATADINE ACTAVIS (CAP), DESLORATADINE RATIOPHARM (CAP), DESLORATADINE TEVA (CAP), NEOCLARITYN (CAP); loratadine (NAP)

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

PRAC Rapporteur: To be appointed

Scope: Signal of weight increase in children

Action: For adoption of PRAC recommendation

EPITT 18906 – New signal

Lead Member State(s): BE

4.3. Signals follow-up and prioritisation

4.3.1. Amoxicillin (NAP)

Applicant(s): various

PRAC Rapporteur: Jan Neuhauser

Scope: Signal of drug rash eosinophilia systemic symptoms (DRESS) syndrome

Action: For adoption of PRAC recommendation

EPITT 18802 – Follow-up to May 2017

4.3.2. Ciprofloxacin (NAP); meropenem (NAP)

Applicant(s): various

PRAC Rapporteur: Jan Neuhauser

Scope: Signal of incompatibility between ciprofloxacin and meropenem when co-administered intravenously leading to possible precipitation

Action: For adoption of PRAC recommendation

EPITT 18790 – Follow-up to March 2017

4.3.3. Darbepoetin alfa – ARANESP (CAP) - EMEA/H/C/000332/SDA/091; epoetin alfa – ABSEAMED (CAP) - EMEA/H/C/000727/SDA/029, BINOCRIT (CAP) - EMEA/H/C/000725/SDA/028, EPOETIN ALFA HEXAL (CAP) - EMEA/H/C/000726/SDA/030, NAP; epoetin beta – NEORECORMON (CAP) - EMEA/H/C/000116/SDA/055; epoetin theta – BIOPOIN (CAP) - EMEA/H/C/0001036/SDA/022, EPORATIO (CAP) - EMEA/H/C/0001033/SDA/022; epoetin zeta – RETACRIT (CAP) - EMEA/H/C/000872/SDA/046, SILAPO (CAP) - EMEA/H/C/000760/SDA/039, methoxy polyethylene glycol-epoetin beta – MIRCERA (CAP) - EMEA/H/C/000739/SDA/039; NAP

Applicants: Amgen Europe B.V. (Aranesp), Hexal AG (Epoetin Alfa Hexal), Hospira UK Limited (Retacrit), Medice Arzneimittel Pütter GmbH & Co. KG (Abseamed), Roche Registration Limited (Neorecormon, Mircera), Ratiopharm GmbH (Eporatio), Sandoz GmbH (Binocrit), Stada Arzneimittel AG (Silapo), Teva GmbH (Biopoin); various

PRAC Rapporteur: Valerie Strassmann

Scope: Signal of severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)

Action: For adoption of PRAC recommendation

EPITT 18846 – Follow-up to February 2017

4.3.4. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/SDA/012.1

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 March 2017

4.3.5. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/SDA/023.1; BYETTA (CAP) - EMEA/H/C/000698/SDA/043.1

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of incorrect use of device associated with (serious) adverse reactions including hyperglycaemia and hypoglycaemia

Action: For adoption of PRAC recommendation

EPITT 18688 – Follow-up to February 2017

4.3.6. Fulvestrant - FASLODEX (CAP) - EMEA/H/C/000540/SDA/028

Applicant(s): AstraZeneca UK Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of anaphylactic reactions

Action: For adoption of PRAC recommendation

EPITT 18832 – Follow-up to March 2017

4.3.7. Intravenous (IV) fluids containing electrolytes and/or carbohydrates (NAP)

Applicant(s): various

PRAC Rapporteur: Doris Stenver

Scope: Signal of hyponatremia

Action: For adoption of PRAC recommendation

EPITT 18631 – Follow-up to June 2017

4.3.8. Prednisolone (NAP); prednisone (NAP)

Applicant(s): various

PRAC Rapporteur: Doris Stenver

Scope: Signal of induced scleroderma renal crisis

Action: For adoption of PRAC recommendation

EPITT 18888 – Follow-up to June 2017

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Adalimumab - EMEA/H/C/004319

Scope: Treatment of rheumatoid arthritis, axial spondyloarthritis, psoriasis, hidradenitis suppurativa (HS), Crohn’s disease, ulcerative colitis and uveitis

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

5.1.2. Buprenorphine, naloxone - EMEA/H/C/004407

Scope: Treatment for opioid drug dependence

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

5.1.3. Carmustine - EMEA/H/C/004326

Scope: Treatment of brain tumours, multiple myeloma, Hodgkin's and non-Hodgkin’s lymphomas

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

5.1.4. Dupilumab - EMEA/H/C/004390

Scope: Treatment of moderate-to-severe atopic dermatitis

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

5.1.5. Fluticasone furoate, umeclidinium, vilanterol - EMEA/H/C/004781

Scope: Treatment of adult patients with chronic obstructive pulmonary disease (COPD)

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

5.1.6. Fluticasone furoate, umeclidinium, vilanterol - EMEA/H/C/004363

Scope: Treatment of adult patients with chronic obstructive pulmonary disease (COPD)

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

5.1.7. Guselkumab - EMEA/H/C/004271

Scope: Treatment of plaque psoriasis

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

5.1.8. Letermovir - EMEA/H/C/004536, Orphan

Applicant: Merck Sharp & Dohme Limited

Scope accelerated assessment: Treatment and prophylaxis of cytomegalovirus (CMV) reactivation and disease

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

5.1.9. Naloxone - EMEA/H/C/004325

Scope: Treatment in emergency use for known or suspected opioid overdose as manifested by respiratory and/or central nervous system depression

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

5.1.10. Neratinib - EMEA/H/C/004030

Scope: Treatment and extended adjuvant treatment of adult patients with early-stage human epidermal growth factor receptor 2 (HER2)-overexpressed, amplified breast cancer who have received prior adjuvant trastuzumab based therapy

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

5.1.11. Padeliporfin - EMEA/H/C/004182

Scope: Treatment of prostate cancer

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

5.1.12. Ritonavir - EMEA/H/C/004549

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

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

5.1.13. Tacrolimus - EMEA/H/C/004435

Scope: Treatment of allograft rejection and prophylaxis of transplant rejection

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

5.1.14. Trastuzumab - EMEA/H/C/004323

Scope: Treatment of breast cancer and metastatic gastric cancer

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

5.2. Medicines in the post-authorisation phase – PRAC-led procedures

5.2.1. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/WS1169/0028; Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/WS1169/0032

Applicant: AbbVie Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the RMPs for Exviera (version 3.0) and Viekirax (version 3.0) following the CHMP opinion dated 15 December 2016 (EMA/CHMP/847450/2016) on the procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free) in order to implement 'hepatitis B reactivation' as an important identified risk, 'emergence of hepatocellular carcinoma' and 'recurrence of hepatocellular carcinoma' as important potential risks, 'patients with previous hepatocellular carcinoma (HCC)' as missing information. The requested studies have also been reflected in the RMPs accordingly

Action: For adoption of PRAC Assessment Report

5.2.2. Dapagliflozin – EBYMECT (CAP)- EMEA/H/C/004162/WS1198/0022; EDISTRIDE (CAP) - EMEA/H/C/004161/WS1198/0017; FORXIGA (CAP) - EMEA/H/C/002322/WS1198/0037; XIGDUO (CAP) - EMEA/H/C/002672/WS1198/0033

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMPs for Ebymect (version 13.3), Edistride (version 13.3), Forxiga (version 13.3), Xigduo (version 13.3) following the finalisation in February 2017 (EMEA/H/A-20/1442) of the procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputations

Action: For adoption of PRAC Assessment Report

5.2.3. Fidaxomicin - DIFICLIR (CAP) - EMEA/H/C/002087/II/0028

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP (version 7) in order to remove the post-authorisation measure (PAM) MEA003 regarding clinical study 2819-CL-2001: an open-label, prospective, interventional study in adult patients who received a second treatment course of fidaxomicin to treat a recurrent *Clostridium difficile* infection (CDI) that developed within 3 months after completion of an initially successful treatment of a primary CDI with fidaxomicin, due to the non-feasibility of the study

Action: For adoption of PRAC Assessment Report

5.2.4. Interferon beta-1a - REBIF (CAP) - EMEA/H/C/000136/II/0129

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP (version 9.0) in order to upgrade the important potential risk 'immunogenicity/safety risk associated with the formation of neutralizing antibodies' to an important identified risk

Action: For adoption of PRAC Assessment Report

5.2.5. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0049

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Update of the RMP (version 17) in order to amend the study objectives and milestones for two studies: 1) study CA184332 (a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab (Yervoy) as first line therapy in a community setting, a category 3 study in the RMP (MEA 029): to submit the final study report with 2-years of follow-up); 2) study CA184338 (a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab (Yervoy) as first line therapy, a category 3 study in the RMP (MEA 030): to submit the final study report with 4-years of follow-up)

Action: For adoption of PRAC Assessment Report

5.2.6. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/WS1163/0051; Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS1163/0041

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of the RMPs for Harvoni (version 6.0) and Sovaldi (version 6.0) following the CHMP opinion dated 15 December 2016 (EMA/CHMP/847450/2016) on the procedure under

Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free) in order to implement 'hepatitis B reactivation' as an important identified risk, 'emergence of hepatocellular carcinoma' and 'recurrence of hepatocellular carcinoma' as important potential risks, 'patients with previous hepatocellular carcinoma (HCC)' as missing information. The requested studies have also been reflected in the RMPs accordingly

Action: For adoption of PRAC Assessment Report

5.2.7. Turoctocog alfa - NOVOEIGHT (CAP) - EMEA/H/C/002719/II/0020

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of the RMP (version 3) and submission of an amended protocol for PASS study NN7008-3553 (a multicentre non-interventional study of safety and efficacy of turoctocog alfa (rFVIII) during long-term treatment of severe and moderately severe haemophilia a (FVIII =<2%), a category 3 study in the RMP) to update the milestone timelines in order to integrate the required additional pharmacovigilance activities, which include a change in the last patient last visit (LPLV) date and a change in the clinical trial report (CTR) finalisation date. In addition, the duration of the trial has been amended from 4 to 7 years

Action: For adoption of PRAC Assessment Report

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

5.3.1. Abiraterone acetate - ZYTIGA (CAP) - EMEA/H/C/002321/II/0047

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer and in combination with androgen deprivation therapy. 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 14.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

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

5.3.2. 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. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/II/0017

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and long term use information in the posology following final results from study CAMMS03409: an extension protocol for multiple sclerosis (MS) patients who participated in Genzyme-sponsored studies of alemtuzumab to evaluate the long term safety and efficacy of alemtuzumab in MS patients who received alemtuzumab during prior company-sponsored studies. The Package Leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to bring the Product Information in line with the latest QRD template (version 10.0) and to introduce editorial corrections

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

5.3.4. Anakinra - KINERET (CAP) - EMEA/H/C/000363/II/0056

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Torbjorn Callreus

Scope: Extension of indication to include a new indication for Kineret 100 mg/0.67 ml solution for injection in pre-filled syringe for the treatment of active Still's disease, including systemic juvenile idiopathic arthritis and adult-onset Still's disease. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 4.0) are updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the SmPC and package leaflet

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

5.3.5. Autologous $CD34^+$ enriched cell fraction that contains $CD34^+$ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) complementary deoxyribonucleic acid (cDNA) sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/II/0006, Orphan

Applicant: GlaxoSmithKline Trading Services, ATMP[5]

PRAC Rapporteur: Sabine Straus

Scope: Quality -Sections 4.3 and 4.4 of the SmPC are updated. The RMP (version 1.6) is updated accordingly. The MAH took the opportunity to introduce some editorial changes in Annex II and III-B of the product information

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

[5] Advanced therapy medicinal product

5.3.6. Baricitinib – OLUMIANT (CAP) – EMEA/H/C/004085/II/0001

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Update of section 4.4 of the SmPC in order to add a warning on venous thromboembolism based on analyses of the occurrence of venous thromboembolic events in clinical trials with baricitinib. The Package Leaflet and the RMP (version 2.0) are updated accordingly

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

5.3.7. Bortezomib - BORTEZOMIB ACCORD (CAP) - EMEA/H/C/003984/X/0008

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Line extension application to add a new strength of powder for solution for injection (1 mg) to the currently approved strength (3.5 mg) of Bortezomib Accord. The RMP (version 6.0) is updated accordingly

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

5.3.8. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0048, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of adult patients with $CD30^+$ cutaneous T-cell lymphoma (CTCL) who require systemic therapy, based on data from study C25001 ('ALCANZA' study): a phase 3 trial of brentuximab vedotin (SGN-35) versus physician's choice (methotrexate or bexarotene) in patients with cd30-positive cutaneous t-cell lymphoma. 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 10) are updated accordingly

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

5.3.9. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/II/0141

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on severe cutaneous conditions including erythema multiforme, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) following a request for a cumulative review as per the PRAC signal recommendation dated February 2017 (EPITT 18846). The Package Leaflet and the RMP (version 7) are updated accordingly

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

5.3.10. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/II/0142

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Extension of indication to include the treatment of anaemia in adult patients with low transfusion demand in low or intermediate-1-risk myelodysplastic syndromes for Aranesp. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to update the safety and efficacy information. The Package Leaflet and the RMP (version 8.0) are updated accordingly. In addition, the MAH took the opportunity to introduce QRD editorial changes in the SmPC, Annex III-A and Annex III-B

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

5.3.11. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0055

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with multiple myeloma and in adults with bone metastases from solid tumours' for Xgeva. 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 24.0) are updated accordingly

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

5.3.12. 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 body weight of at least 25 kg, infected with human immunodeficiency virus-1 (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 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

5.3.13. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/X/0029

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Line extension to add new pharmaceutical form and strengths (film-coated tablets

40 mg and 80 mg) to the currently approved presentations for Xtandi. The RMP (version 10.1) is updated accordingly

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

5.3.14. Human normal immunoglobulin - PRIVIGEN (CAP) - EMEA/H/C/000831/II/0119

Applicant: CSL Behring GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.8 and 5.1 to implement the results of the PATH (IgPro20_3003) study results: a randomized, multicentre, double-blind, placebo-controlled, parallel-group phase 3 study to investigate the efficacy, safety, and tolerability of two different doses of IgPro20 (subcutaneous immunoglobulin) for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP). In addition, the MAH took the opportunity to implement a clarification on the hyperprolinemia types in section 4.3 and to introduce some editorial changes to section 5.2 of the SmPC. 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

5.3.15. Idarucizumab - PRAXBIND (CAP) - EMEA/H/C/003986/II/0007

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the final results from study 1321.3, the RE-VERSE-AD study (re-versal effects of idarucizumab on active dabigatran): a phase 3 case series clinical study of the reversal of the anticoagulant effects of dabigatran by intravenous administration of 5.0 g idarucizumab (BI 655075) in patients treated with dabigatran etexilate who have uncontrolled bleeding or require emergency surgery or procedures - RMP category 3 study (MEA 001)). The RMP (version 3.0) is updated accordingly. In addition, the MAH took the opportunity to update the immunogenicity section in 5.1 of SmPC and to bring the product information (PI) in line with the latest QRD template (version 10)

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

5.3.16. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/II/0008, Orphan

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the clinical study report (CSR) for study E7080-J081-208: a phase 2 multicentre, open-label, single-arm study to evaluate the safety of once daily oral administration of lenvatinib (E7080) in subjects with advanced thyroid cancer

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

5.3.17. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/X/0020

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

Scope: Line extension application to add a new strength of film-coated tablets (100 mg lumacaftor/125 mg ivacaftor) for paediatric use from the age of 6 to 11 years. The RMP (version 3.1) is updated accordingly

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

5.3.18. Lurasidone - LATUDA (CAP) - EMEA/H/C/002713/II/0016

Applicant: Sunovion Pharmaceuticals Europe Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final clinical study report (CSR) for study D1001057: an extension of study SM-13496 (lurasidone): a phase 3, randomized, double-blind, parallel-group, placebo-controlled, confirmatory study evaluating the long-term safety and efficacy of lurasidone (40 mg/day or 80 mg/day) in patients with schizophrenia. The RMP (version 5.0) is updated with information relative to this study and information relative to study D1050301 already assessed in P46/006

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

5.3.19. Miglustat - ZAVESCA (CAP) - EMEA/H/C/000435/II/0056, Orphan

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the eighth Niemann-Pick type C (NPC) registry report and update of Annex II-D of the product information to delete the NPC Registry listed as an obligation to the marketing authorisation. The RMP (version 12.1) is updated accordingly. In addition, the MAH took the opportunity to introduce minor changes and bring the Product Information and Annex A in line with the latest QRD template (version 10)

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

5.3.20. Oseltamivir - TAMIFLU (CAP) - EMEA/H/C/000402/II/0128

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Update of section 4.6 of the SmPC in order to reflect the final study results from a non-interventional safety study BV29684, which assessed the safety of oseltamivir exposure in pregnant women (RMP category 3 study (MEA099)). The RMP (version 15.0) is updated accordingly

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

See also under 10.3.2.

5.3.21. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0016

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Submission of the final clinical study report (CSR) for study Aura 17: a phase 2, open label, single-arm study to assess the safety and efficacy of AZD9291 in Asia pacific patients with locally advanced/metastatic non-small cell lung cancer whose disease has progressed with previous epidermal growth factor receptor tyrosine kinase inhibitor therapy and whose tumours harbour a T790M mutation within the epidermal growth factor receptor gene). The RMP (version 7.0) is updated accordingly

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

5.3.22. Pegaspargase - ONCASPAR (CAP) - EMEA/H/C/003789/X/0008

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Patrick Batty

Scope: Line extension application to add a new pharmaceutical form, powder for solution for injection/infusion (750 U/mL). The RMP (version 2.0) is updated accordingly

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

5.3.23. Peginterferon alfa-2a - PEGASYS (CAP) - EMEA/H/C/000395/II/0091

Applicant: Roche Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to include paediatric patients from 3 to less than 18 years of age with chronic hepatitis B in the immune-active phase for Pegasys. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add efficacy and safety information from study YV25718: a phase 3b parallel group, open label study of pegylated interferon alfa-2a monotherapy compared to untreated control in children with HBeAg positive chronic hepatitis B. 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

5.3.24. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0029

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Submission of the final study report for a non-clinical study 'anti-murine PD-1 antibody (muDX400 L-005571333): an exploratory multiple-dose subcutaneous immunotoxicity study in mice with hepatitis B vaccine (L-005552770)'. The RMP (version 11.0) is updated accordingly

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

5.3.25. Plerixafor - MOZOBIL (CAP) - EMEA/H/C/001030/II/0032, Orphan

Applicant: Genzyme Europe BV

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to reflect the results of the completed study MSC12830 (MOZ11809): 'a phase 4, multicentre, randomized, comparator trial evaluating the standard weight-based dose (0.24 mg/kg) compared to a fixed dose (20 mg) of plerixafor injection in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize and collect ≥5 x 10^6 $CD34^+$ cells/kg in ≤4 days and to evaluate the difference in total systemic exposure in patients with non-Hodgkin's lymphoma weighing ≤70 kg' listed as a category 3 study in the RMP. The Package Leaflet and the RMP (version 9.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

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

5.3.26. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - SYNFLORIX (CAP) - EMEA/H/C/000973/II/0117

Applicant: GSK Biologicals SA

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to reflect the results from study 10PN-PD-DIT-072: a phase 3, open, controlled, multicentric study to evaluate the immunogenicity, safety and reactogenicity of Synflorix in children at an increased risk of pneumococcal infection. The Package Leaflet and the RMP (version 16) are updated accordingly. This submission fulfils the post-authorisation measure MEA 065

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

5.3.27. Rilpivirine - EDURANT (CAP) - EMEA/H/C/002264/II/0024

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPC in order to include information on the use of rilpivirine in combination with a background regimen for the treatment of human immunodeficiency virus (HIV)-1 infection during pregnancy and postpartum, without dose adjustment following final results from study TMC114HIV3015 (a single arm, open-label trial to assess the pharmacokinetics of darunavir/ritonavir, etravirine, and rilpivirine in HIV-1-infected pregnant women) listed as a category 3 study in the RMP. The Package Leaflet and the RMP (version 7.0) are updated accordingly. In addition, the MAH took the opportunity to introduce the latest renewal date in section 9 of the SmPC and the physical address of the Netherlands local representative in the Package Leaflet

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

5.3.28. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/II/0052/G

Applicant: Bayer AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations consisting of: 1) addition to the authorised indications: treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults, to Xarelto 10 mg. The RMP (version 10) is updated. 2) change in pack sizes of the finished product: change in the number of units in a pack. 3) change in immediate packaging of the finished product: change in type of container or addition of a new container- solid, semi-solid and non-sterile liquid pharmaceutical forms; 4) addition of information on interactions with selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) in section 4.5 and a related warning in section 4.4 of the SmPC. In addition, MedDRA[6] terminology is updated in the adverse drug reactions; 5) deletion of 'patients undergoing major orthopaedic surgery other than elective hip or knee replacement surgery' and 'remedial pro-coagulant therapy for excessive haemorrhage' from the summary of safety concerns

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

5.3.29. Roflumilast - DALIRESP (CAP) - EMEA/H/C/002398/X/0031

Applicant: AstraZeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: Line extension application to add a new strength of 250 µg in a polyvinyl chloride (PVC)/ polyvinylidine chloride (PVDC)/aluminium (Alu) blister of 28 tablets. The RMP (version 18) is updated accordingly

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

5.3.30. Roflumilast - DAXAS (CAP) - EMEA/H/C/001179/X/0035

Applicant: AstraZeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: Line extension application to add a new strength of 250 µg in a polyvinyl chloride (PVC)/ polyvinylidine chloride (PVDC)/aluminium (Alu) blister of 28 tablets. The RMP (version 18) is updated accordingly

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

5.3.31. Roflumilast - LIBERTEK (CAP) - EMEA/H/C/002399/X/0032

Applicant: AstraZeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: Line extension application to add a new strength of 250 µg in a polyvinyl chloride (PVC)/ polyvinylidine chloride (PVDC)/aluminium (Alu) blister of 28 tablets. The RMP (version 18) is updated accordingly

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

[6] Medical Dictionary for Regulatory Activities

5.3.32. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/II/0009

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Julie Williams

Scope: Update of section 4.5 of the SmPC to add information on the effect of selexipag administration on the pharmacokinetics of midazolam, its metabolite 1-hydroxymidazolam and the CYP3A4[7] metabolism, based on data from the completed clinical pharmacology study AC-065-114: 'a single-centre, open-label, randomized, two-treatment crossover phase 1 study investigating the effect of selexipag on the pharmacokinetics of midazolam and its metabolite 1-hydroxymidazolam in healthy male subjects'. The RMP (version 5.1) is updated to add the results of study AC-065-114, reclassify 'hyperthyroidism' as an important identified risk and update the PASS timelines and protocol versions in accordance with the current EXPOSURE (PASS AC-065A401m: an observational cohort study of pulmonary arterial hypertension (PAH) patients newly treated with either selexipag or any other PAH-specific therapy, in clinical practice) protocol (version 3) and the EDUCATE (PASS AC-065A403,: an evaluation of risk minimisation measures for medication errors with selexipag during the titration phase in patients with PAH in clinical practice) protocol (version 2)

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

5.3.33. Siltuximab - SYLVANT (CAP) - EMEA/H/C/003708/II/0023, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report for study CNTO328SMM2001 listed as a category 3 study in the RMP: 'a phase 2, randomized, double-blind, placebo-controlled, multicentre study of siltuximab (anti interleukin-6 (IL-6) monoclonal antibody) in subjects with high-risk smoldering multiple myeloma' to evaluate immunogenicity data. No changes to the product information (PI) are proposed. The RMP (version 23.0) is updated accordingly

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

5.3.34. Simeprevir - OLYSIO (CAP) - EMEA/H/C/002777/II/0031

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Update of section 5.1 of the SmPC in order to update the efficacy information following results from study HPC3002, a prospective 3-year follow-up study in subjects previously treated in a phase IIb or phase III study with a TMC435-containing regimen for the treatment of hepatitis C virus (HCV) infection listed as a category 3 study in the RMP and in fulfilment of MEA005. The RMP (version 4.0) is updated accordingly and includes updates of changes already agreed in procedures II/0021, II/0027 and EMEA/H/A-20/1438/C/2777/0019

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

[7] Cytochrome P450 3A4

5.3.35. Sirolimus - RAPAMUNE (CAP) - EMEA/H/C/000273/II/0164

Applicant: Pfizer Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of patients with lymphangioleiomyomatosis. As a consequence section 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 6.0) are updated accordingly. In addition, the MAH took the opportunity to make very minor formatting changes in the Labelling

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

5.3.36. Sonidegib - ODOMZO (CAP) - EMEA/H/C/002839/II/0011

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Submission of the final results from study CLDE225C2301: a phase 2, multicentre, open-label, single-arm study of the efficacy and safety of oral LDE225 in patients with Hegehog (Hh)-signalling pathway activated relapsed medulloblastoma, and study LDE225X2104. a phase 1/2 study of sonidegib (LDE225) in paediatric patients with recurrent or refractory medulloblastoma or other tumours potentially dependent on the Hh-signalling pathway and adult patients with recurrent or refractory medulloblastoma. The RMP (version 6.0) is updated accordingly

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

5.3.37. Sunitinib - SUTENT (CAP) - EMEA/H/C/000687/II/0065

Applicant: Pfizer Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: Extension of indication to include the adjuvant treatment of patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated based on study A6181109: 'a randomized double-blind phase 3 study of adjuvant sunitinib *vs*. placebo in subjects at high risk of recurrent RCC'. The Package Leaflet and the RMP (version 16) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes to the SmPC and Package Leaflet. This procedure fulfils PAM (FU2 22.5). Furthermore, the product information (PI) is brought in line with the latest QRD template (version 10)

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

5.3.38. Tedizolid phosphate - SIVEXTRO (CAP) - EMEA/H/C/002846/II/0019

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of section 4.8 of the SmPC of Sivextro concentrate for solution for infusion formulation in order to add information from study BAY119-2631/16121: a phase 3

randomized, double-blind, multicentre study comparing the efficacy and safety of intravenous to oral 6-day tedizolid phosphate and intravenous to oral 10 day linezolid for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and change the reported expected frequency of the adverse reaction 'infusion site phlebitis' from 'uncommon' to 'common'. The Package Leaflet is updated accordingly. The RMP (version 3.0) is also updated and includes a proposal to collect safety information regarding tedizolid phosphate by conducting three investigator initiated studies and deleting the original proposed long term safety study. The MAH also took the opportunity to make minor editorial corrections throughout the product information

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

5.3.39. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/II/0006

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of section 5.1 of the SmPC based on final results from study 156-08-271 (TEMPO 4:4) listed as a PAES in Annex II. This study is a multicentre, open-label, extension study (extension of trial 156-04-251) to evaluate the long-term efficacy and safety of oral tolvaptan tablet regimens in patients with autosomal dominant polycystic kidney disease (ADPKD) over 5 years. Annex II and the RMP (version 13.1) are updated accordingly to reflect the completion of 156-08-271 study. In addition, the MAH took the opportunity to add the current anatomical therapeutic chemical (ATC) code applicable for tolvaptan as assigned by WHO[8]

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

5.3.40. Tolvaptan - SAMSCA (CAP) - EMEA/H/C/000980/X/0024

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Line extension to add a new strength of 7.5 mg tablets. The RMP (version 13.0) is updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Afamelanotide - SCENESSE (CAP) - PSUSA/00010314/201612

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Valerie Strassmann

[8] World Health Organization

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Amifampridine - FIRDAPSE (CAP) - PSUSA/00000141/201612

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Blinatumomab - BLINCYTO (CAP) - PSUSA/00010460/201612

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Clofarabine - EVOLTRA (CAP) - PSUSA/00000805/201612

Applicant: Genzyme Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - PSUSA/00010028/201612

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Daclatasvir - DAKLINZA (CAP) - PSUSA/00010295/201701

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Efmoroctocog alfa - ELOCTA (CAP) - PSUSA/00010451/201612

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Erlotinib - TARCEVA (CAP) - PSUSA/00001255/201611

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Fondaparinux - ARIXTRA (CAP) - PSUSA/00001467/201612

Applicant: Aspen Pharma Trading Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Human fibrinogen, human thrombin - EVARREST (CAP); EVICEL (CAP); RAPLIXA (CAP); TACHOSIL (CAP) - PSUSA/00010297/201612

Applicant: Omrix Biopharmaceuticals N. V. (Evarrest, Evicel), Mallinckrodt Pharmaceuticals Ireland Limited (Raplixa), Takeda Austria GmbH (TachoSil)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Human papillomavirus 9-valent vaccine (recombinant, adsorbed) - GARDASIL 9 (CAP) - PSUSA/00010389/201612

Applicant: MSD Vaccins

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Hydroxocobalamin[9] - CYANOKIT (CAP) - PSUSA/00010228/201611

Applicant: Serb SA

[9] Only for products for chemical poisoning

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Indacaterol - HIROBRIZ BREEZHALER (CAP); ONBREZ BREEZHALER (CAP); OSLIF BREEZHALER (CAP) - PSUSA/00001730/201611 (with RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - PSUSA/00001742/201612

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Lenalidomide - REVLIMID (CAP) - PSUSA/00001838/201612

Applicant: Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Lesinurad - ZURAMPIC (CAP) - PSUSA/00010470/201612

Applicant: Grunenthal GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Liraglutide - SAXENDA (CAP); VICTOZA (CAP) - PSUSA/00001892/201612

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Lutetium (^{177}Lu) chloride - ENDOLUCINBETA (CAP); LUMARK (CAP) - PSUSA/00010391/201612

Applicant: ITG Isotope Technologies Garching GmbH (EndolucinBeta), I.D.B. Holland B.V. (Lumark)

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Lutropin alfa - LUVERIS (CAP) - PSUSA/00001918/201611

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Matrix-applied characterised autologous cultured chondrocytes - MACI (CAP) - PSUSA/00010116/201612

Applicant: Vericel Denmark ApS, ATMP[10]

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.21. Nivolumab - OPDIVO (CAP) - PSUSA/00010379/201701

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Nonacog gamma - RIXUBIS (CAP) - PSUSA/00010320/201612

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Olaparib - LYNPARZA (CAP) - PSUSA/00010322/201612

Applicant: AstraZeneca AB

[10] Advanced therapy medicinal product

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Omalizumab - XOLAIR (CAP) - PSUSA/00002214/201612

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Opicapone - ONGENTYS (CAP) - PSUSA/00010516/201612

Applicant: Bial - Portela & Cª, S.A.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Pancreas powder[11] - ENZEPI (CAP) - PSUSA/00010522/201612

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Pegvisomant - SOMAVERT (CAP) - PSUSA/00002328/201611

Applicant: Pfizer Limited

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Plerixafor - MOZOBIL (CAP) - PSUSA/00002451/201612

Applicant: Genzyme Europe BV

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[11] Centrally authorised product only

6.1.29. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - 10 valent - SYNFLORIX (CAP) - PSUSA/00009262/201612

Applicant: GSK Biologicals SA

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Ponatinib - ICLUSIG (CAP) - PSUSA/00010128/201612

Applicant: Incyte Biosciences UK Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Saquinavir - INVIRASE (CAP) - PSUSA/00002684/201612

Applicant: Roche Registration Limited

PRAC Rapporteur: Marianne Lunzer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Secukinumab - COSENTYX (CAP) - PSUSA/00010341/201612

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Selexipag - UPTRAVI (CAP) - PSUSA/00010503/201612

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Sofosbuvir - SOVALDI (CAP) - PSUSA/00010134/201612

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - PSUSA/00010524/201612

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/201612

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/201701

Applicant: Vanda Pharmaceuticals Ltd.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Tedizolid phosphate - SIVEXTRO (CAP) - PSUSA/00010369/201612

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Ticagrelor - BRILIQUE (CAP) - PSUSA/00002948/201612 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Umeclidinium bromide, vilanterol - ANORO (CAP); LAVENTAIR (CAP) - PSUSA/00010264/201612

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Ustekinumab - STELARA (CAP) - PSUSA/00003085/201612

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

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. Clopidogrel - CLOPIDOGREL ZENTIVA (CAP), ISCOVER (CAP), PLAVIX (CAP); clopidogrel, acetylsalicylic acid - CLOPIDOGREL/ACETYLSALICYLIC ACID ZENTIVA (CAP), DUOPLAVIN (CAP); NAP - PSUSA/00000820/201611

Applicant(s): Sanofi-aventis groupe (Clopidogrel Zentiva, Clopidogrel/Acetylsalicylic acid Zentiva, Iscover), Sanofi Clir SNC (DuoPlavin, Plavix), various

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Bosentan - STAYVEER (CAP); TRACLEER (CAP); NAP - PSUSA/00000425/201611

Applicant(s): Marklas Nederlands BV (Stayveer), Actelion Registration Ltd. (Tracleer), various

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Human hepatitis B immunoglobulin - ZUTECTRA (CAP); NAP - PSUSA/00001631/201611

Applicant(s): Biotest Pharma GmbH (Zutectra), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

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. Allergen for diagnostic: skin prick test containing only Phleum pratense[12] - PSUSA/00010466/201610

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Apomorphine (NAP) - PSUSA/00000227/201611

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Benzalkonium chloride, chlorhexidine digluconate (NAP) - PSUSA/00010070/201611

Applicant(s): various

PRAC Lead: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Calcium salts, colecalciferol (NAP) - PSUSA/00010386/201610

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Chloroquine phosphate, proguanil hydrochloride (NAP) - PSUSA/00010207/201611

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[12] Product(s) authorised via mutually recognition procedure (MRP) only

6.3.6. Clevidipine (NAP) - PSUSA/00010288/201611

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Domperidone (NAP) - PSUSA/00001158/201611

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Ethinylestradiol, norgestimate (NAP) - PSUSA/00001313/201610

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Human coagulation factor VII (NAP) - PSUSA/00001619/201610

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Hydroxycarbamide[13] (NAP) - PSUSA/00009182/201612

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Isoflurane (NAP) - PSUSA/00001786/201610

Applicant(s): various

PRAC Lead: Julia Pallos

[13] Centrally authorised product(s) excluded

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Isotretinoin[14] (NAP) - PSUSA/00010488/201611

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Lacidipine (NAP) - PSUSA/00001815/201610

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Lenograstim (NAP) - PSUSA/00001839/201610

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Magnesium hydroxide (NAP) - PSUSA/00001926/201610

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Methoxyflurane (NAP) - PSUSA/00010484/201611

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[14] Oral formulations

6.3.17. Teicoplanin (NAP) - PSUSA/00002878/201611

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Tixocortol (NAP); chlorhexidine gluconate, tixocortol pivalate (NAP) - PSUSA/00010333/201611

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Treprostinil (NAP) - PSUSA/00003013/201611

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Oseltamivir - TAMIFLU (CAP) - EMEA/H/C/000402/LEG 104.1

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to LEG 104 [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] as per the request for supplementary information (RSI) adopted in March 2017

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[15]

7.1.1. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/PSA/S/0019

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsova

Scope: Substantial amendment to the protocol for study 20150136: 'an observational study of blinatumomab safety and effectiveness, utilisation, and treatment practices', as previously agreed in the conclusions of procedure EMEA/H/C/PSP/0041.1 adopted by PRAC in September 2016

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

7.1.2. Cidofovir (NAP) - EMEA/H/N/PSP/S/0052.1

Applicant: Emcure Pharma UK Ltd (Cidofovir Emcure Pharma)

PRAC Rapporteur: Julie Williams

Scope: Revised protocol for 'a non-interventional, prospective, exposure (safety outcome) registry study of cidofovir to further elucidate the characteristics of the different patient populations for cidofovir use, gather details of adverse events and patient outcome following treatment in a specified indication' as per the conclusion of procedure EMEA/H/N/PSP/S/0052 adopted by PRAC in February 2017

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

7.1.3. Levonorgestrel (NAP) - EMEA/H/N/PSA/S/0020

Applicant: Bayer Pharma AG (Jaydess, Luadei)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Substantial amendment to the previously agreed protocol (version 2.2) for EURAS-LCS12 study: a European active surveillance study of LCS-12 (levonorgestrel intrauterine contraceptive system releasing 12 mcg levonorgestrel/24h in vitro), an intra-uterine device (IUD) for Jaydess and Luadei (levonorgestrel) to investigate whether LCS-12 is associated with an increased risk of unintended pregnancy compared to Mirena and to copper IUDs (previous conclusions of procedure EMEA/H/N/PSA/j/0006.1 adopted by PRAC in September 2016)

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

7.1.4. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/PSA/S/0018

Applicant: Bayer AG

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

PRAC Rapporteur: Qun-Ying Yue

Scope: Substantial amendment to the previously agreed protocol for an observational post-authorisation safety specialist cohort event monitoring study (SCEM) to monitor the safety and utilisation of Xarelto (rivaroxaban) initiated in secondary care for the prevention of atherothrombotic events in patients who have had acute coronary syndrome in England and Wales (previous conclusions of procedure EMEA/H/C/PSP/0026 adopted by PRAC in June 2015)

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

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

7.2.1. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 005.1

Applicant: Celgene Europe Limited

PRAC Rapporteur: Eva Segovia

Scope: Revised PASS protocol in order to collect long-term data using the PsoBest registry, as per the request for supplementary information (RSI) agreed in the conclusions of procedure EMEA/H/C/003746/MEA 005 adopted in September 2015

Action: For adoption of advice to CHMP

7.2.2. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/MEA 001

Applicant: Ipsen Pharma

PRAC Rapporteur: Sabine Straus

Scope: PASS protocol for study F-FR-60000-001: a non-interventional prospective study exploring the utilisation of cabozantinib in subjects with advanced renal cell carcinoma (RCC) following prior vascular endothelial growth factor (VEGF)-targeted therapy in real life settings in terms of dose modifications due to adverse events (AEs) when used as a second line therapy or third and later line therapy

Action: For adoption of advice to CHMP

7.2.3. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/MEA 003

Applicant: Roche Registration Limited

PRAC Rapporteur: Sabine Straus

Scope: Protocol for study ML939302 (COVENIS): a non-interventional study to investigate the effectiveness, safety and utilisation of cobimetinib and vemurafenib in patients with and without brain metastasis with BRAF V600 mutant melanoma under real world conditions (study completion planned in Q4/2020)

Action: For adoption of advice to CHMP

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

7.2.4. Daclizumab - ZINBRYTA (CAP) - EMEA/H/C/003862/MEA 003

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia

Scope: Protocol for study 205MS407: a phase 4 observational study in the European Economic Area (EEA) to evaluate the effectiveness of physician hepatic risk management guide as an additional risk minimisation measure in patients prescribed Zinbryta using health insurance claims or patient electronic medical records

Action: For adoption of advice to CHMP

7.2.5. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/MEA 016.1

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Patrick Batty

Scope: Revised PASS protocol for study GS-EU-313-4226: a cross-sectional PASS to assess healthcare professional (HCP) awareness of risks associated with Zydelig in the European Union (EU) as per the request for supplementary information (RSI) agreed in the conclusion of procedure EMEA/H/C/003843/MEA 016 adopted in March 2017

Action: For adoption of advice to CHMP

7.2.6. Levetiracetam - KEPPRA (CAP) - EMEA/H/C/000277/MEA 086

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Protocol for PASS study EPD172 comparing the incidence of renal failure in patients with epilepsy exposed to levetiracetam or other antiepileptic drugs (final study report: 31 December 2017)

Action: For adoption of advice to CHMP

7.2.7. Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/MEA 001.4

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Revised protocol for study 178-CL-114: evaluation of cardiovascular events in users of mirabegron and other treatments for overactive bladder as per the request for supplementary information agreed in the conclusions of procedure EMEA/H/C/002388/MEA 001.4 adopted in March 2017

Action: For adoption of advice to CHMP

7.2.8. Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/MEA 009

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Protocol for PASS study 178-PV-002: a drug utilisation study (DUS) of Betmiga (mirabegron) using real-world healthcare databases from the Netherlands, Spain, United Kingdom and Finland

Action: For adoption of advice to CHMP

7.2.9. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/MEA 256.10

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Caroline Laborde

Scope: Amendment to protocol for study GS-EU-104-0433: a drug utilisation study (DUS) in human immunodeficiency virus (HIV)-1 and hepatitis B virus (HBV) infected paediatric patients to follow-up the effectiveness of the agreed risk minimisation measures, further to the request for supplementary information (RSI) adopted in the conclusions of EMEA/H/C/000419/MEA 256.9 on the second interim report assessment adopted in March 2017

Action: For adoption of advice to CHMP

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

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

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

PRAC Rapporteur: Valerie Strassmann

Scope: MAH's response to EMEA/H/N/PSR/J/0007 [final study results for an imposed non-interventional PASS EUPAS11134: a retrospective chart review to evaluate the effectiveness of the risk minimisation measures for the use of flupirtine 100 mg immediate-release capsules in daily practice] as per the request for supplementary information (RSI) adopted by PRAC in March 2017

Action: For adoption of recommendation to CMDh

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

7.4.1. Adalimumab - AMGEVITA (CAP) - EMEA/H/C/004212/WS1182/0001; Adalimumab - SOLYMBIC (CAP) - EMEA/H/C/004373/WS1182/0001

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report for study 20130258: an open-label, single-arm extension study to evaluate the long-term safety and efficacy of ABP 501 in subjects with moderate to severe rheumatoid arthritis, listed as a category 3 study in the RMP (MEA002).

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

The RMP (version 2.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0049/G

Applicant: Pfizer Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped variations consisting of: 1) submission of the final report for a non-interventional PASS study A8081049: a cross-sectional study to evaluate the effectiveness of Xalkori (crizotinib) therapeutic management guide among physicians prescribing Xalkori in Europe. In the light of the study results, the MAH proposed to update Annex II to remove the Xalkori TMG from the educational materials; 2) submission of the final study report for PASS study A8081050, a cross-sectional study to evaluate the effectiveness of Xalkori patient information brochure among non-small cell lung cancer (NSCLC) patients receiving Xalkori treatment in Europe. The MAH also took the opportunity to state 'monotherapy' in section 4.1 of the SmPC as requested by the CHMP and to bring the product information (PI) in line with the latest QRD template

Action: For adoption of PRAC Assessment Report

7.4.3. Epoetin zeta - RETACRIT (CAP) - EMEA/H/C/000872/II/0077

Applicant: Hospira UK Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Submission of the final report from the registry based healthcare database study HDBS study linked to PASCO (PMS-830-07-0043: a post-authorisation safety cohort observation of Retacrit (epoetin zeta) for the treatment of renal anaemia) listed as a category 3 study in the RMP. This is an observational study on the incidence of thromboembolic events in patients with renal anaemia treated with erythropoietin zeta as compared with erythropoietin alfa and other erythropoiesis-stimulating agents (ESA)

Action: For adoption of PRAC Assessment Report

7.4.4. Epoetin zeta - SILAPO (CAP) - EMEA/H/C/000760/II/0045

Applicant: Stada Arzneimittel AG

PRAC Rapporteur: Valerie Strassmann

Scope: Submission of the final report from the registry based healthcare database study HDBS study linked to PASCO (PMS-830-07-0043: a post-authorisation safety cohort observation of Silapo (epoetin zeta) for the treatment of renal anaemia) listed as a category 3 study in the RMP. This is an observational study on the incidence of thromboembolic events in patients with renal anaemia treated with erythropoietin zeta as compared with erythropoietin alfa and other erythropoiesis-stimulating agents (ESA). The RMP (version 11) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/WS1188/0157; LIPROLOG (CAP) - EMEA/H/C/000393/WS1188/0120

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report for a non-interventional PASS EUPAS 13422 aiming at evaluating the impact of additional risk minimisation measures on healthcare professionals and on patients' understanding and their behaviour regarding the risk of hypoglycaemia and/or hyperglycaemia due to medication errors associated with administration of Humalog 200 U/mL KwikPen or Liprolog 200 U/mL KwikPen

Action: For adoption of PRAC Assessment Report

7.4.6. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0095, Orphan

Applicant: Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of the final results of the non-interventional, observational category 3 PASS study CC-5013-PASS-001 in subjects treated with lenalidomide to further characterise the safety profile of lenalidomide plus dexamethasone in the treatment of relapsed and/or refractory (R/R) multiple myeloma (MM) in a real-world setting

Action: For adoption of PRAC Assessment Report

7.4.7. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/II/0101

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final clinical study report (CSR) for TYGRIS: a post-marketing safety observational cohort programme designed to obtain long-term safety data (approximately 5 years) in subjects with multiple sclerosis (MS) treated with natalizumab, and comprising parallel studies 101MS402 (United States and Canada) and 101MS403 (rest of the World). The RMP (version 23) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. Rufinamide - INOVELON (CAP) - EMEA/H/C/000660/II/0041, Orphan

Applicant: Eisai Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of the final clinical study report (CSR) for study E2080-E044-401: a European registry of anti-epileptic drug use in patients with Lennox-Gastaut syndrome (LGS), listed as a category 3 study in the RMP, in fulfilment of MEA 002.1. E2080-E044-401 is a non-interventional EU registry study entering patients (aged ≥4 years) with LGS who required a modification in anti-epileptic therapy (either the addition of another anti-epileptic drugs (AED) or the change of one drug to another) in order to evaluate the long-term safety of rufinamide

Action: For adoption of PRAC Assessment Report

7.4.9. Zoledronic acid - ACLASTA (CAP) - EMEA/H/C/000595/II/0069

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final 5-year report from study (ZOL446H2422) listed as a category 3 study in the RMP: a non-interventional post-authorisation safety study using health registries to compare safety of Aclasta against oral bisphosphonates and untreated population controls

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 053.4

Applicant: Genzyme Europe BV

PRAC Rapporteur: Caroline Laborde

Scope: MAH's response to MEA 053.3: revised first interim study report [epidemiology PASS study report for study ALGMYC07390 evaluating the prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions] as per the request for supplementary information (RSI) adopted by PRAC in March 2017

Action: For adoption of advice to CHMP

7.5.2. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.2

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Two-yearly interim report on study PTC124-GD-025o-DMD: a post-approval registry observational study exploring the long-term of ataluren safety and effectiveness in usual care setting (RMP category 3 study) (three year interim report due on 30 April 2018)

Action: For adoption of advice to CHMP

7.5.3. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/MEA 010.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

Scope: Second interim results (semi-annual report) for a category 3 study TMC207TBC4002: a multinational prospective multidrug resistant tuberculosis (MDRTB) patient registry to monitor bedaquiline safety, utilisation, and emergence of resistance (final study report: Q2 2020)

Action: For adoption of advice to CHMP

7.5.4. Data collection on adverse events of anti-HIV[19] drugs (D:A:D) study - PRAC evaluation of D:A:D data merger results

Applicant(s): various

PRAC Representatives: Filip Josephson, Deborah Ashby

Scope: Evaluation of the seventeenth data merger

Action: For adoption of advice to CHMP

7.5.5. Dabrafenib - TAFINLAR (CAP) - EMEA/H/C/002614/MEA 013

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual report (integrated safety analysis report) for clinical studies: 1) BRF113683 (BREAK-3): a two-arm, open-label, randomized Phase III pivotal study comparing oral dabrafenib with intravenous dacarbazine (DTIC), 2) MEK115306 (COMBI-d): a two-arm, double-blinded, randomized, Phase III study comparing dabrafenib and trametinib combination therapy (to be referred to as combination therapy in this report) with dabrafenib administered with a trametinib placebo (dabrafenib monotherapy) and 3) MEK116513 (COMBI-v): a 2-arm, randomized, open-label, Phase III study comparing dabrafenib and trametinib combination therapy with vemurafenib monotherapy in BRAF V600 mutation-positive metastatic melanoma on secondary malignancies in patients treated with dabrafenib in randomised controlled trials to comply with the additional pharmacovigilance activity as requested in the RMP. The report identifies and characterises the risk of treatment-emergent cutaneous and non-cutaneous malignancies in randomised controlled clinical trials of dabrafenib; alone or in combination with other anticancer drugs

Action: For adoption of advice to CHMP

7.5.6. Degarelix - FIRMAGON (CAP) - EMEA/H/C/000986/MEA 013.2

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Ghania Chamouni

Scope: Sixth annual progress report (data cut-off date: 18 February 2017) for PASS FE 200486 CS39: a prospective observational safety study in patients with advanced prostate cancer treated with Firmagon (degarelix) or a gonadotropin-releasing hormone (GnRH) agonist

Action: For adoption of advice to CHMP

7.5.7. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/ANX 005.2

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Patrick Batty

[19] Human immunodeficiency virus

Scope: Third annual study report (reporting period: 14 February 2016 to 13 February 2017) for the multicentre, multinational, observational Morquio A registry study (MARS): a voluntary observational registry study to characterise and describe the mucopolysaccharidosis IV type A (MPS IVA) population and to evaluate the long-term effectiveness and safety of Vimizim (elosulfase alfa) (final clinical study report (CSR): March 2025)

Action: For adoption of advice to CHMP

7.5.8. Meningococcal group B vaccine (rDNA, component, adsorbed) - BEXSERO (CAP) - EMEA/H/C/002333/MEA 023

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: First progress report of Bexsero pregnancy registry: an observational study of the safety of Bexsero exposure in pregnant women and their offspring

Action: For adoption of advice to CHMP

7.5.9. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/MEA 256.11

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Caroline Laborde

Scope: MAH's response [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] to the request for supplementary information (RSI) adopted in the conclusions of EMEA/H/C/000419/MEA 256.9 in March 2017

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 006.7

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: Bi-annual status reports for study DNE3001/CREDENCE: a randomized, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with type 2 diabetes mellitus and diabetic nephropathy) from the Independent Data Monitoring Committee (IDMC) (IDMC report dated March 2017)

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 005.7

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Bi-annual status reports for study DNE3001/CREDENCE: a randomized, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with type 2 diabetes mellitus and diabetic nephropathy) from the Independent Data Monitoring Committee (IDMC) (IDMC report dated March 2017)

Action: For adoption of advice to CHMP

7.6.3. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/LEG 058.1

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to LEG 058 [evaluation of Increlex growth forum database (EU-IGFD) post-marketing surveillance: a multicentre, open-label, non- interventional study based in Europe (ENCEPP/SDPP/7708) collecting long term safety and effectiveness data on mecasermin] as per the request for supplementary information adopted by CHMP in December 2016

Action: For adoption of advice to CHMP

7.6.4. Telavancin - VIBATIV (CAP) - EMEA/H/C/001240/ANX 007.5

Applicant: Theravance Biopharma Ireland Ltd

PRAC Rapporteur: Julie Williams

Scope: Submission of a pregnancy exposure follow-up questionnaire in the context of the pregnancy exposure registry (9809-CL-1409), as per the request for supplementary information (RSI) adopted in the conclusions of procedure EMEA/H/C/001240/ANX 007.4 adopted in September 2016

Action: For adoption of advice to CHMP

7.6.5. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/LEG 031

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: Review on causality assessment and analysis of hypotension cases

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. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/S/0070 (without RMP)

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Patrick Batty

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. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/R/0013 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Conditional renewal of the of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/R/0051 (with RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/R/0003 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Olaratumab - LARTRUVO (CAP) - EMEA/H/C/004216/R/0004 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.5. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/R/0005 (without RMP)

Applicant: AbbVie Ltd.

PRAC Rapporteur: Patrick Batty

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Aflibercept - ZALTRAP (CAP) - EMEA/H/C/002532/R/0037 (without RMP)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Florbetapir (^{18}F) - AMYVID (CAP) - EMEA/H/C/002422/R/0026 (with RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Ibandronic acid - IBANDRONIC ACID ACCORD (CAP) - EMEA/H/C/002638/R/0013 (without RMP)

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Doris Stenver

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Imatinib - IMATINIB TEVA (CAP) - EMEA/H/C/002585/R/0028 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Insulin degludec - TRESIBA (CAP) - EMEA/H/C/002498/R/0027 (without RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Insulin degludec, insulin aspart - RYZODEG (CAP) - EMEA/H/C/002499/R/0024 (with RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Lixisenatide - LYXUMIA (CAP) - EMEA/H/C/002445/R/0023 (with RMP)

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Qun-Ying Yue

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Meningococcal group B vaccine (rDNA, component, adsorbed) - BEXSERO (CAP) - EMEA/H/C/002333/R/0053 (without RMP)

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/R/0026 (with RMP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

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

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

10.3.1. Capecitabine - XELODA (CAP) - EMEA/H/C/000316/LEG 033.1

Applicant: Roche Registration Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of responses, including a CHMP Pharmacogenomics Working Party (PgWP) report dated March 2017, to the proposal of a group of academic and clinical experts put forward to the CHMP and PRAC to review the SmPCs of fluoropyrimidines (Xeloda (capecitabine) and 5-fluorouracil (5FU)) and suggesting that screening for dihydropyriminidine dehydrogenase (DPYD) variants and relevant dose reduction in patients taking fluoropyrimidines could reduce the risk of toxicity in patients with dihydropyrimidine dehydrogenase deficiency

Action: For adoption of advice to CHMP

10.3.2. Oseltamivir - TAMIFLU (CAP) - EMEA/H/C/000402/II/0128

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Update of section 4.6 of the SmPC in order to reflect the final study results from a non-interventional safety study BV29684, which assessed the safety of oseltamivir exposure in pregnant women (RMP category 3 study (MEA099)). The RMP (version 15.0) is updated accordingly

Action: For adoption of advice to CHMP

See also under 5.3.20.

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

11.2.1. Flupirtine (NAP)

Applicant(s): Meda (DUS), Teva (PASS, DUS)

PRAC Lead: Martin Huber

Scope: PRAC consultation on the evaluation of final study results for 1) a PASS (Teva): a multicentre, non-interventional, retrospective chart review study of patients treated with flupirtine-containing medicinal products in Germany comparing two 6-months periods before and after implementation of the risk minimisation measures (RMM) following the referral procedure for flupirtine-containing products (EMEA/H/A-107i/1363); 2) a drug utilisation study (DUS) (Teva): a retrospective cohort analysis of the IMS disease analyser database for four separate annual time intervals (2012-2015) in Germany before and after implementation of the RMM following the referral procedure; 3) a DUS (Meda) (DE/H/3034/1/II/007): a retrospective DUS conducted in an outpatient setting in Germany using an electronic medical record database (IMS disease analyser) and a prescription database (IMS LRx) to describe the prescription behaviour during one time period before and two time periods after the implementation of the risk minimisation measures following the referral procedure

Action: For adoption of advice to Member States

11.2.2. Lacosamide - DE/H/4720/001-004/DC, DE/H/4726/001-004/DC, DE/H/4830/001-004/DC, DE/H/4831/001-004/DC, DE/H/4832-4834/001-004/DC, DE/H/4835/001-004/DC, DE/H/4841/001-004/DC, DE/H/4842/001-004/DC

PRAC Lead: Martin Huber

Scope: PRAC consultation on the evaluation of initial marketing authorisation applications under the decentralised procedure for lacosamide-generic medicinal products on request of Germany

Action: For adoption of advice to Member States

11.2.3. Levonorgestrel[20] (NAP)

Applicant(s): Bayer (Mirena, Jaydess)

PRAC Lead: Martin Huber

Scope: PRAC consultation on the evaluation of cumulative reviews on levonorgestrel IUS and possible interaction with lamotrigine, the risk of arthralgia and the risk of breast discharge as requested in the conclusions of procedure PSUSA/00001856/201412 adopted in September 2015, on request of Germany

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC Brexit ancillary working group

PRAC lead: Almath Spooner

Action: For discussion

12.1.2. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of qualitative goals

PRAC lead: Martin Huber, Menno van der Elst, Tatiana Magalova, Albert van der Zeijden, Marianne Lunzer, Jan Neuhauser, Ulla Wändel Liminga

Action: For discussion

[20] Intrauterine system (IUS) only

12.2. Coordination with EMA Scientific Committees or CMDh

12.2.1. Advanced therapy medicinal products (ATMP) - Revision of procedural advice on the evaluation of ATMP in accordance with Article 8 of Regulation (EC) No 1394/2007

Action: For discussion

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. European Network Training Centre (EU NTC) - operation of pharmacovigilance in the EU training needs and priorities

PRAC lead: Dolores Montero Corominas

Action: For adoption

12.4.2. Innovative Medicines Initiative (IMI) WEB-Recognising Adverse Drug Reactions (WEB-RADR) project – Pharmacovigilance and social media – Work package 1: policy and governance deliverable

PRAC lead: June Raine

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan for 2017 - update

PRAC lead: June Raine

Action: For discussion

12.8. Planning and reporting

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

Action: For discussion

12.8.2. Marketing authorisation applications (MAA) expected for 2017 – Q2 2017 update

Action: For discussion

12.8.3. PRAC workload statistics – Q2 2017

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

None

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

12.11.1. Good Pharmacovigilance Practice (GVP) module IX on Signal management – revision 1 and addendum

PRAC lead: Sabine Straus

Action: For discussion

12.11.2. 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. Guideline on detection and management of duplicate individual cases and individual case safety reports (ICSRs) – revision 1

Action: For adoption

12.12.2. Good Pharmacovigilance Practice (GVP) module VI on Management and reporting of adverse reactions to medicinal products - revision 2

Action: For adoption

12.12.3. Management and reporting of adverse reactions to medicinal products

None

12.12.4. Additional monitoring

None

12.12.5. 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. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.16.2. Referral procedures: pilot phase for abolition of signatures for divergent positions

Action: For discussion

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. Industry stakeholder platform on the operation of the EU pharmacovigilance – Feedback from the eleventh industry stakeholder platform meeting held on 2 June 2017

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/