27 November 2017
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Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 27-30 November 2017

Chair: June Raine – Vice-Chair: Almath Spooner

27 November 2017, 13:00 – 19:30, room 3/A

28 November 2017, 08:30 – 19:30, room 3/A

29 November 2017, 08:30 – 19:30, room 3/A

30 November 2017, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

14 December 2017, 09:00-12:00, room 7/B, via teleconference

Health and safety information

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

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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, Rev. 1).

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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 27-30 November 2017. See December 2017 PRAC minutes (to be published post January 2018 PRAC meeting).

1.2. Agenda of the meeting on 27-30 November 2017

Action: For adoption

1.3. Minutes of the previous meeting on 23-26 October 2017

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

2.2.1. Hydroxyethyl starch (HES)[1] (NAP)

Applicants: Fresenius Kabi Deutschland GmbH (Volulyte, Voluven), B. Braun Melsungen AG (Tetraspan, Venofundin), Seruwerk Bernburg AG (Hesra); various

PRAC Rapporteur: Patrick Batty; PRAC Co-rapporteur: Ulla Wändel Liminga

Scope: Review of the benefit-risk balance following notification by Sweden of a referral under Article 107i of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption of a list of experts (LoE) for an ad-hoc expert group meeting

2.3. Procedures for finalisation

None

[1] Solution for infusion

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

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

Applicant(s): Eisai Ltd (Panretin, Targretin), various

PRAC Rapporteur: Ana Sofia Diniz Martins; PRAC Co-rapporteur: Julie Williams

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

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

3.2.2. 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 outstanding issues (LoOI)

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

3.4.1. Paracetamol[3] (NAP); paracetamol, tramadol[4] (NAP) - EMEA/H/A-31/1445

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

PRAC Rapporteur: Željana Margan Koletić; PRAC Co-rapporteur: Adam Przybylkowski

[2] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[3] Modified release formulations
[4] Modified release formulations

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

Action: For adoption of a recommendation to CMDh

3.5. Others

None

4. Signals assessment and prioritisation[5]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Daratumumab – DARZALEX (CAP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of cytomegalovirus (CMV) reactivation

Action: For adoption of PRAC recommendation

EPITT 19087 – New signal

Lead Member State: PT

4.1.2. Nivolumab – OPDIVO (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of tumour lysis syndrome

Action: For adoption of PRAC recommendation

EPITT 19086 – New signal

Lead Member State: DE

4.1.3. Human normal immunoglobulin – FLEBOGAMMA DIF (CAP), HIZENTRA (CAP), HYQVIA (CAP), KIOVIG (CAP), PRIVIGEN (CAP); NAPs

Applicant(s): Baxalta Innovations GmbH (HyQvia), Baxter AG (Kiovig), CSL Behring GmbH (Privigen, Hizentra), Instituto Grifols, S.A. (Flebogamma DIF)

PRAC Rapporteur: To be appointed

[5] 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

Scope: Signal of lupus-like syndrome and related terms

Action: For adoption of PRAC recommendation

EPITT 19098 – New signal

Lead Member State: DE

4.1.4. Vortioxetine – BRINTELLIX (CAP)

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Laurence de Fays

Scope: Signal of angioedema

Action: For adoption of PRAC recommendation

EPITT 19099 – New signal

Lead Member State: BE

4.2. New signals detected from other sources

4.2.1. Dasatinib – SPRYCEL (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Doris Stenver

Scope: Signal of cytomegalovirus (CMV) reactivation

Action: For adoption of PRAC recommendation

EPITT 19111 – New signal

Lead Member State: DK

4.2.2. Lapatinib – TYVERB (CAP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of pulmonary hypertension

Action: For adoption of PRAC recommendation

EPITT 19089 – New signal

Lead Member State: SE

4.2.3. Radium (^{223}Ra) dichloride - XOFIGO (CAP)

Applicant: Bayer AG

PRAC Rapporteur: Patrick Batty

Scope: Signal of fractures and fatal cases in chemotherapy-naïve patients

Action: For adoption of PRAC recommendation

EPITT 19132 – New signal

Lead Member State: UK

4.3. Signals follow-up and prioritisation

4.3.1. Insulin[6]: insulin aspart – NOVOMIX (CAP) - EMEA/H/C/000308/SDA/054, NOVORAPID (CAP)- EMEA/H/C/000258/SDA/047; insulin bovine (NAP); insulin degludec – TRESIBA (CAP) - EMEA/H/C/002498/SDA/011; insulin degludec, insulin aspart – RYZODEG (CAP) - EMEA/H/C/002499/SDA/006, insulin degludec, liraglutide – XULTOPHY (CAP) - EMEA/H/C/002647/SDA/003; insulin detemir – LEVEMIR (CAP) - EMEA/H/C/000528/SDA/052; insulin glargine – ABASAGLAR (CAP) - EMEA/H/C/002835/SDA/004, LANTUS (CAP) - EMEA/H/C/000284/SDA/053, LUSDUNA (CAP) - EMEA/H/C/004101/SDA/002, TOUJEO (CAP) - EMEA/H/C/000309/SDA/052; insulin glulisine – APIDRA (CAP) - EMEA/H/C/000557/SDA/041; insulin human (rDNA) – ACTRAPHANE (CAP) - EMEA/H/C/000427/SDA/024, ACTRAPID (CAP) - EMEA/H/C/000424/SDA/025, INSULATARD (CAP), INSULIN HUMAN WINTHROP (CAP) - EMEA/H/C/000761/SDA/008, INSUMAN (CAP) - EMEA/H/C/000201/SDA/048, MIXTARD (CAP) - EMEA/H/C/000428/SDA/026, PROTAPHANE (CAP) - EMEA/H/C/000442/SDA/028; insulin human, insulin isophane (NAP); insulin lispro – HUMALOG (CAP) - EMEA/H/C/000088/SDA/031, LIPROLOG (CAP) - EMEA/H/C/000393/SDA/024; insulin porcine (NAP)

Applicant(s): Eli Lilly Regional Operations GmbH (Abasaglar); Eli Lilly Nederland B.V. (Humalog, Liprolog); Novo Nordisk A/S (Actraphane, Actrapid, Insulatard, Levemir, Mixtard, NovoMix, NovoRapid, Protaphane, Ryzodeg, Tresiba, Xultophy); Merck Sharp & Dohme Limited (Lusduna); Sanofi-aventis Deutschland GmbH (Apidra, Lantus, Toujeo, Insulin Human Winthrop, Insuman); various

PRAC Rapporteur: Julie Williams

Scope: Signal of potential increased risk of medication error associated with withdrawing insulin from pre-filled pens and cartridges, leading to dysglycaemia

Action: For adoption of PRAC recommendation

EPITT 18893 – Follow-up to October 2017

4.3.2. mTOR[7] inhibitors: everolimus – AFINITOR (CAP) - EMEA/H/C/001038/SDA/030, VOTUBIA (CAP) - EMEA/H/C/002311/SDA/030, NAP; sirolimus – RAPAMUNE (CAP) - EMEA/H/C/000273/SDA/053; temsirolimus – TORISEL (CAP) - EMEA/H/C/000799/SDA/037

Applicant(s): Novartis Europharm Ltd (Afinitor, Votubia), Pfizer Limited (Rapamune, Torisel), various

PRAC Rapporteur: Martin Huber

Scope: Signal of optic neuropathy and papilloedema

[6] Pre-filled pens and cartridges
[7] Mechanistic target of rapamycin

Action: For adoption of PRAC recommendation

EPITT 18901 – Follow-up to June 2017

4.3.3. Phenprocoumon (NAP)

Applicant: various

PRAC Rapporteur: Martin Huber

Scope: Signal related to risk of birth defects and foetal loss following first trimester exposure as a function of the time of withdrawal

Action: For adoption of PRAC recommendation

EPITT 18902 – Follow-up to June 2017

4.3.4. Ritonavir - NORVIR (CAP) - EMEA/H/C/000127/SDA/050; lopinavir, ritonavir – KALETRA (CAP) – EMEA/H/C/000368/SDA/120; levothyroxine (NAP)

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

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC recommendation

EPITT 18896 – Follow-up to July 2017

4.3.5. Tofacitinib – XELJANZ (CAP) – EMEA/H/C/004214/SDA/005

Applicant(s): Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Signal of angioedema

Action: For adoption of PRAC recommendation

EPITT 18904 – Follow-up to July 2017

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Axicabtagene ciloleucel - EMEA/H/C/004480, Orphan

Applicant: Kite Pharma EU B.V.; ATMP[8]

Scope (accelerated assessment): Treatment of diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL)

[8] Advanced therapy medicinal product

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

5.1.2. Efavirenz, emtricitabine, tenofovir disoproxil - EMEA/H/C/004274

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

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

5.1.3. Eteplirsen - EMEA/H/C/004355, Orphan

Applicant: Avi Biopharma International Ltd

Scope: Treatment of Duchenne muscular dystrophy

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

5.1.4. Gemtuzumab ozogamicin - EMEA/H/C/004204, Orphan

Applicant: Pfizer Limited

Scope: Treatment of adult patients with previously untreated, de novo acute myeloid leukaemia (AML), combination therapy with daunorubicin (DNR) and cytarabine (AraC)

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

5.1.5. Metreleptin - EMEA/H/C/004218, Orphan

Applicant: Aegerion Pharmaceuticals Limited

Scope: Treatment of leptin deficiency (lipodystrophy)

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

5.1.6. Pegfilgrastim - EMEA/H/C/004413

Scope: Treatment of neutropenia

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

5.1.7. Prasugrel - EMEA/H/C/004644

Scope: Treatment and prevention of atherothrombotic events

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

5.1.8. Voretigene neparvovec - EMEA/H/C/004451, Orphan

Applicant: Spark Therapeutics Ireland Ltd; ATMP[9]

Scope: Treatment of patients with vision loss due to Leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy

[9] Advanced therapy medicinal product

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. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/WS1164/0033; Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/WS1164/0008; Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/WS1164/0030

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Updated RMPs (Jardiance (version 12.1), Glyxambi (version 3.0), Synjardy (version 9.2)) to reflect changes requested in the PRAC recommendation for the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442). In addition, the RMPs are updated to include pancreatitis as an important potential risk for empagliflozin-containing medicines following the PRAC recommendation for the PSUSA procedure for canagliflozin-containing products (PSUSA/00010077/201603) adopted in October 2016

Action: For adoption of PRAC Assessment Report

5.2.2. Ofatumumab - ARZERRA (CAP) - EMEA/H/C/001131/II/0054, Orphan

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Updated RMP (version 14.0) to reflect changes in the pharmacovigilance activities pertaining to the timelines of study OMB112517 (PROLONG study): a phase 3, open label, randomised, multicentre trial of ofatumumab maintenance treatment versus no further treatment in subjects with relapsed chronic lymphocytic leukaemia (CLL) who have responded to induction therapy; as well as to study OMB110913 (Complement 2): a phase 3, open label, randomised trial of ofatumumab added to fludarabine-cyclophosphamide *vs* fludarabine-cyclophosphamide combination in subjects with relapsed CLL. In addition, changes have been implemented in the safety specifications as previously agreed with CHMP

Action: For adoption of PRAC Assessment Report

5.2.3. Pioglitazone - ACTOS (CAP) - EMEA/H/C/000285/WS1294/0078; GLUSTIN (CAP) - EMEA/H/C/000286/WS1294/0077; pioglitazone, glimepiride - TANDEMACT (CAP) - EMEA/H/C/000680/WS1294/0056 pioglitazone, metformin - COMPETACT (CAP) - EMEA/H/C/000655/WS1294/0068; GLUBRAVA (CAP) - EMEA/H/C/000893/WS1294/0055

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: Updated RMPs for Actos, Glustin (version 24.0), Tandemact (version 22.0), Competact and Glubrava (version 25.0) to reflect a bone mechanistic addendum report for

study AD4833-402: a randomised, double-blind, placebo-controlled, multicentre study to evaluate the effect of pioglitazone on bone mass and metabolism in postmenopausal women with impaired fasting plasma glucose. In addition, the RMPs for Competact and Glubrava, are updated to include the lactic acidosis questionnaire as requested in the conclusions of variations EMEA/H/C/000655/WS0991/0062 and EMEA/H/C/000893/WS0991/0047 adopted in January 2017

Action: For adoption of PRAC Assessment Report

5.2.4. Telbivudine - SEBIVO (CAP) - EMEA/H/C/000713/II/0048

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Caroline Laborde

Scope: Updated RMP (version 11.0) in order to reclassify the risk of lactic acidosis from an important potential risk to an important identified risk and to include a targeted questionnaire for fatal cases as additional risk minimisation measure as requested by the PRAC as part of the assessment of PSUSA/00002880/201608 adopted in April 2017

Action: For adoption of PRAC Assessment Report

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

5.3.1. Adalimumab - IMRALDI (CAP) - EMEA/H/C/004279/II/0002/G

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Quality grouped variations. The RMP (version 2.0) is updated accordingly. The MAH also took the opportunity to introduce some editorial changes to the product information

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

5.3.2. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/II/0037, Orphan

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include a new population: children from 2 to less than 5 years of age. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP (version 7.1) are updated accordingly

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

5.3.3. Atazanavir, cobicistat - EVOTAZ (CAP) - EMEA/H/C/003904/WS1292/0019; atazanavir - REYATAZ (CAP) - EMEA/H/C/000494/WS1292/0114

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Caroline Laborde

Scope: Update of section 4.3 and 4.5 of the SmPC in order to add a contraindication with

lurasidone to reflect this interaction based on literature data. The Package Leaflet and the RMP (version 14 for Reyataz; version 6 for Evotaz) are updated accordingly

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

5.3.4. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0002/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add myocarditis as a new adverse reaction based on the results of a cumulative review of cases of suspected myocarditis. As a consequence, the information regarding the posology and special warnings have been updated. Annex II, the Package Leaflet and the RMP (version 2.0) have been updated accordingly; 2) update of the RMP to add haemolytic anaemia as a new important potential risk

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

5.3.5. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0003

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Update of section 4.4 of the SmPC in order to include results of a vaccination sub-study of the long term extension study I4V-MC-JADY: a phase 3, multicentre study to evaluate the long-term safety and efficacy of baricitinib in patients with rheumatoid arthritis. The RMP (version 4.0) is updated accordingly

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

5.3.6. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0011, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and amend the safety information. The Labelling and the RMP (version 4.0) are updated accordingly

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

5.3.7. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/II/0003

Applicant: Ipsen Pharma

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include for the treatment of advanced renal cell carcinoma the 'treatment-naïve adults with intermediate or poor risk per IMDC criteria'. As a

consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated in order to add a warning on dose reductions and dose interruptions and to update the safety information. The final report of study A031203: a randomized phase 2 study comparing cabozantinib with commercially supplied sunitinib in patients with previously untreated locally advanced or metastatic renal cell carcinoma is submitted in support of this application. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to introduce some editorial changes in the product information

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

5.3.8. Carfilzomib - KYPROLIS (CAP) - EMEA/H/C/003790/II/0017/G, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Grouped variation consisting of: 1) update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the second interim analysis of the overall survival data from study ENDEAVOR (study 20130398): a randomised, multicentre, open-label, phase 3 study of carfilzomib and dexamethasone compared to bortezomib with dexamethasone in patients with relapse multiple myeloma. The Package Leaflet and the RMP (version 9.0) are updated accordingly; 2) update of section 4.8 of the SmPC in order to revise the frequencies of certain adverse drug reactions based on the pooled data set including ENDEAVOR and seven recently completed studies. In addition, the MAH took the opportunity to add editorial changes in sections 4.2, 4.4, 6.3 and 6.6 of the SmPC. Several editorial changes are also included in the package leaflet and labelling

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

5.3.9. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0050

Applicant: Pfizer Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Update of sections 4.2, 4.3, 4.4, 4.8 and 5.2 of the SmPC in order to update the information about hepatic impairment based on the results of study A8081012: a phase 1 study evaluating the effect of hepatic impairment on the pharmacokinetics and safety of crizotinib in advanced cancer patients. The package leaflet and the RMP (version 7.4) are updated accordingly. The final study report of study A8081012 is included

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

5.3.10. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/II/0026, Orphan

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the frequencies of adverse reactions included in the tabulated list of adverse reactions and to update the clinical efficacy and safety information based on the results from study 2006-05 (listed as category 3 in the RMP): a phase 3, open-label expanded access study designed to provide access to defibrotide as an investigational new drug to patients with severe hepatic veno-

occlusive disease. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to bring the SmPC in line with the latest QRD template (version 10), to update the list of local representatives in the package leaflet and to correct a translation error in the Polish, Finnish, Danish and Latvian versions

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

5.3.11. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0022

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.2, 5.1 and 5.2 of the SmPC following completion of a phase 3 study H9X-MCGBDX (GBDX) comparing the effect of once-weekly Trulicity with insulin glargine on glycaemic control over 52 weeks in patients with type 2 diabetes mellitus (T2DM) and moderate or severe chronic kidney disease. In addition, an update to the anatomical therapeutic chemical (ATC) code and a correction to section 6.6 of the SmPC are introduced. The RMP (version 1.11) is updated accordingly

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

5.3.12. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0098, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.6 and 5.3 of the SmPC in order to update the safety information related to pregnancy, lactation and fertility following the review of data in PSUR#13 and PSUR#14. Annex II, the Package Leaflet and the RMP (version 17) are updated accordingly

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

5.3.13. Eliglustat - CERDELGA (CAP) - EMEA/H/C/003724/II/0015/G, Orphan

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: Grouped variations consisting of an update of sections 4.2, 4.3, 4.4, 4.5 and 5.2 of the SmPC based on the final data from: 1) study POP13777: an open-label pharmacokinetic and tolerability study of eliglustat tartrate given as a single dose in subjects with mild and moderate hepatic impairment, and in matched subjects with normal hepatic function (MEA003.3) and; 2) study POP13778: an open-label two-stage pharmacokinetic and tolerability study of eliglustat tartrate given as a single dose in subjects with mild, moderate and severe renal impairment, and in matched subjects with normal renal function (MEA004.3). Annex II D, 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

5.3.14. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/II/0135

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to include pre-exposure prophylaxis of human immunodeficiency virus (HIV) infection in adolescents aged 12 to < 18 years at high risk. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated based on extrapolation of data for emtricitabine, tenofovir disoproxil fumarate, and Truvada in HIV-infected and uninfected subjects. The Package Leaflet and the RMP (version 15) are updated accordingly. In addition, the MAH took the opportunity to introduce minor linguistic amendments to the Product Information

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

5.3.15. Enoxaparin sodium - INHIXA (CAP) - EMEA/H/C/004264/X/0018

Applicant: Techdow Europe AB

PRAC Rapporteur: Menno van der Elst

Scope: Extension application to add two new strengths of 12,000 IU (120 mg)/0.8 mL and 15,000 IU (150 mg)/1 mL for enoxaparin sodium solution for injection in pre-filled syringe, for subcutaneous, extracorporeal and intravenous administration. The RMP (version 2) is updated accordingly

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

5.3.16. Evolocumab - REPATHA (CAP) - EMEA/H/C/003766/II/0017/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped variation consisting of an extension of indication to include the reduction of atherosclerotic cardiovascular disease risk in adults with high cardiovascular risk based on the results from study 20110118: a double-blind, randomized, placebo-controlled, multicentre study assessing the impact of additional low-density lipoprotein (LDL)-cholesterol reduction on major cardiovascular events when evolocumab (AMG 145) is used in combination with statin therapy in patients with clinically evident cardiovascular disease (category 3 pharmacovigilance activity in the RMP, MEA 004). As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update section 5.1 of the SmPC to include important mechanistic information for healthcare professionals based on study 20120153 (a double-blind, randomized, multicentre, placebo-controlled, parallel group study to determine the effects of evolocumab (AMG 145) treatment on stherosclerotic disease burden as measured by intravascular ultrasound in subjects undergoing coronary catheterisation, a category 3 pharmacovigilance activity, MEA 006). The RMP (version 2.0) is also updated in order to add two category 3 studies in the RMP (study 20160250: a multicentre, open-label, single-arm, extension study to assess long-term safety of evolocumab therapy in subjects with clinically evident cardiovascular disease in selected European countries and study 20150338: a multicentre, controlled, open-label extension (OLE) study to assess the long-term safety and efficacy of evolocumab (AMG 145)) as well

as to update the milestones of five category 3 studies (study 20110110: multicentre, controlled, OLE study to assess the long-term safety and efficacy of evolocumab; study 20110271: multicentre, open-label study to assess the long-term safety, tolerability, and efficacy of evolocumab on low-density lipoprotein cholesterol (LDL-C) in subjects with severe familial hypercholesterolaemia (including homozygous familial hypercholesterolemia (HoFH)); study 20120138: a multicentre, controlled, OLE study to assess the long-term safety and efficacy of evolocumab; study 20130286: a double blind, randomized, placebo controlled, multicentre study to evaluate safety, tolerability, and efficacy on LDL-C of evolocumab in human immunodeficiency virus (HIV) positive patients with hyperlipidemia and mixed dyslipidemia; and study 20130295: a multicentre, OLE study to assess long-term safety and efficacy of evolocumab therapy in patients with clinically evident cardiovascular disease (FOURIER-OLE)

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

5.3.17. Ferric maltol - FERACCRU (CAP) - EMEA/H/C/002733/II/0010

Applicant: Shield TX (UK) Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to widen the indication from 'the treatment in adults with iron deficiency anaemia' in patients with inflammatory bowel disease (IBD) to 'the treatment of adults with iron deficiency'. As a consequence, sections 4.1, 4.4, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 8.0) 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

5.3.18. Fidaxomicin - DIFICLIR (CAP) - EMEA/H/C/002087/II/0032/G

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the safety information following final results from study ANEMONE listed as an additional pharmacovigilance activity in the RMP: a drug utilisation study (DUS) of the use of oral fidaxomicin in routine clinical settings. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet; 2) Update of sections 4.4 and 5.2 of the SmPC in order to update the safety information based on results from the PROFILE study: an open label study designed to evaluate the pharmacokinetics of fidaxomicin in inflammatory bowel disease (IBD) subjects with *Clostridium difficile* infection (CDI). The Package Leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.19. Human normal immunoglobulin - HIZENTRA (CAP) - EMEA/H/C/002127/II/0087

Applicant: CSL Behring GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include immunomodulatory therapy for the treatment of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment. 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 4.0) are updated accordingly

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

5.3.20. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/II/0038

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Patrick Batty

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to reflect information from a recent cumulative safety review of cases of organising pneumonia. The Package Leaflet and Labelling are updated accordingly. The RMP (version 2.6) is also updated to extend the deadlines for submission of final clinical study report (CSR) for three studies linked to Annex II conditions

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

See also under 10.1.1.

5.3.21. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0044

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in children and adolescents 12 years of age and older. As a consequence sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 15) are updated accordingly

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

5.3.22. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/II/0063/G, Orphan

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Grouped variations consisting of; 1) extension of indication to include the combination regimen of the ivacaftor 150 mg evening dose and Symkevi (tezacaftor/ivacaftor); to add a blister card pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/005); 2) addition of a blister pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/006). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 6.5 and 8 of the SmPC are updated. Annex A, the Package Leaflet, Labelling and RMP (version 6.0) are updated accordingly

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

5.3.23. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/II/0009

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include alone or in combination with conventional disease-modifying anti-rheumatic drug (cDMARD) the treatment of active psoriatic arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more DMARD therapies. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated to reflect the new safety and efficacy information. The Package Leaflet and the RMP (version 5) are updated accordingly

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

5.3.24. Nitric oxide - INOMAX (CAP) - EMEA/H/C/000337/II/0051

Applicant: Linde Healthcare AB

PRAC Rapporteur: Julie Williams

Scope: Quality variation to introduce an additional container closure system. The RMP (version 6.0) is updated to reflect post-authorisation experience with the new cylinder closure system

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

5.3.25. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0039

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with advanced or recurrent gastric or gastroesophageal junction (GEJ) cancer after two or more prior systemic therapies, based on data from study ONO-4538-12: a Phase 3 study, multicentre, double-blind, randomized study in patients with unresectable advanced or recurrent gastric cancer. As a consequence, sections 4.1, 4.4, 4.8, and 5.1 of the SmPC are updated. Annex II, package leaflet and the RMP (version 11.0) are updated accordingly

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

5.3.26. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/X/0016/G, Orphan

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Grouped application consisting of: 1) extension application (line extension) to add a new pharmaceutical form (film-coated tablets) associated with a new strength (100 mg and 150 mg); 2) Alignment of the Product Information (PI) for the approved capsule presentation with the PI proposed for the tablet presentation. The RMP (version 15) is updated accordingly

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

5.3.27. Palbociclib - IBRANCE (CAP) - EMEA/H/C/003853/II/0007

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: Update of sections 4.2, 4.4 and 5.2 of the SmPC to reflect the results of study A5481013: a phase 1, open-label, single dose 75 mg palbociclib), parallel-cohort study to evaluate the pharmacokinetics of palbociclib in subjects with impaired hepatic function, and study A5481014: a phase 1, open-label, single dose (125 mg palbociclib), parallel-group study to evaluate the pharmacokinetics of palbociclib in subjects with impaired renal function. The RMP (version 1.4) is updated accordingly

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

5.3.28. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/II/0093/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Grouped variations consisting of: 1) addition of a new device: the on-body injector (Onpro kit) to be used with Neulasta, 6mg solution for injection, pre-filled syringe; 2) change the fill volume for Neulasta, 6 mg, solution for injection pre-filled syringe co-packed with the on-body injector (Onpro kit). In addition, the MAH took the opportunity to introduce editorial changes to module 3.2.P.2.4 on container closure system. As a consequence, sections 3, 4.2, 5.1, 6.4, 6.5, 6.6 and 8 of the SmPC are updated. The Labelling, Package Leaflet and the RMP (version 4.2) are updated accordingly. In addition the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to include some editorial changes and correct some typos throughout the product information. Finally, the MAH brought the product information in line with the latest QRD template (version 10)

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

5.3.29. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0037/G

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.4 and 4.8 of the SmPC to add information regarding the risks of encephalitis, sarcoidosis and graft versus host disease (GVHD) that have been reported in patients treated with pembrolizumab. The package leaflet, the 'additional risk minimization measures' section (educational material) in Annex II and the RMP (version 13.0) are updated accordingly. In addition, the MAH has implemented minor changes in the SmPC section 5.1 and editorial changes in the package leaflet

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

5.3.30. Pertuzumab - PERJETA (CAP) - EMEA/H/C/002547/II/0034

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication for Perjeta in combination with trastuzumab and chemotherapy for the adjuvant treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive early breast cancer. The submission is based on the primary analysis of efficacy and safety data from the pivotal Phase 3 study BIG-4-11/BO25126/TOC4939g (APHINITY): a randomized multicentre, double-blind, placebo-controlled comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer. The MAH also aims to fulfil Annex IID obligation from the approval of the neoadjuvant indication of Perjeta granted in 2015. As a consequence, sections 4.2, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Annex II, the Package Leaflet and the RMP (version 10.0) are updated accordingly

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

5.3.31. Rituximab - BLITZIMA (CAP) - EMEA/H/C/004723/WS1248/0002/G, RITEMVIA (CAP) - EMEA/H/C/004725/WS1248/0002/G, RITUZENA (CAP) - EMEA/H/C/004724/WS1248/0003/G

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations consisting of addition of a new pack size of 2 vials with a fill weight/fill volume of rituximab concentrate solution for infusion of 100 mg/10 mL to the existing pack size of 1 vial of 500 mg rituximab concentrate for infusion without changing the concentration. A 24 month shelf life of the new vial (rituximab 100 mg concentrate solution for infusion) is proposed, and the new presentation is intended to be single-dose, partial use. The RMP (version 8.0) is updated accordingly

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

5.3.32. 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

5.3.33. 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

5.3.34. 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

5.3.35. Rufinamide - INOVELON (CAP) - EMEA/H/C/000660/II/0045, Orphan

Applicant: Eisai Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: Extension of indication to include the treatment of seizures associated with Lennox Gastaut syndrome in patients of 1 year of age and older as adjunctive therapy. As a consequence, sections 4.1, 4.2, 4.5, 5.1 and 5.2 are updated. The package leaflet and the RMP (version 10.0) are updated accordingly. In addition the MAH took the opportunity to include minor corrections in the product information and to update the name and contact details of the local representative in Belgium and Luxembourg. Furthermore, the product information is brought in line with the latest QRD template version 10

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

5.3.36. Sapropterin - KUVAN (CAP) - EMEA/H/C/000943/II/0052, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Almath Spooner

Scope: Update of section 4.4 of the SmPC to add a warning regarding gastritis and update of section 4.8 to add the following adverse events regarding gastrointestinal tract and respiratory irritation: oropharyngeal pain, oesophageal pain, dyspepsia, nausea, gastritis and pharyngitis. The package leaflet and the RMP (version 13.0) are updated accordingly

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

5.3.37. Siltuximab - SYLVANT (CAP) - EMEA/H/C/003708/II/0026/G, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of an update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the product information following final results from: 1) study CNTO328MCD2001: a randomized, double blind, placebo controlled study to assess the efficacy and safety of siltuximab plus best supportive care compared with best supportive care in subjects with multicentric Castleman's disease;2) study CNTO328MCD2002: an open-label, multicenter study to evaluate the safety of long-term treatment with siltuximab

in subjects with multicentric Castleman's disease, both listed as imposed obligations in Annex II. The package leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.38. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/X/0020

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application (line extension) to add new strengths of 2500 IU, 3000 IU, 4000 IU for Nuwiq, powder and solvent for solution for injection. The RMP (version 5.4) is updated accordingly

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

5.3.39. 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

5.3.40. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0006

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include treatment of adult patients with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying anti-rheumatic drug (DMARD) therapy, based on data from study A3921091: a phase 3, randomized, double-blind, placebo-controlled study of the efficacy and safety of 2 doses of tofacitinib or adalimumab in subjects with active psoriatic arthritis; study A3921092: a long term, open label extension study of tofacitinib for the treatment of psoriatic arthritis); study A3921125: a phase 3, randomized, double-blind, placebo-controlled study of the efficacy and safety of 2 doses of tofacitinib in subjects with active psoriatic arthritis and an inadequate response to at least one tumour necrosis factor (TNF) inhibitor. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated accordingly. In

addition, the MAH took the opportunity to update Annex II with minor editorial changes

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

5.3.41. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/X/0005/G

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Grouped variations consisting of: 1) extension application (line extension) to introduce a new strength (10 mg film coated tablets); 2) extension of indication to include 'the induction and maintenance of treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent'. The RMP (version 2.0) is updated accordingly

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

5.3.42. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/II/0028

Applicant: Genzyme Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Update of sections 4.1, 4.4 and 5.1 of the SmPC in order to delete the information regarding rearranged during transfection (RET) mutation. The application fulfils SOB 001 and includes a proposal to revert from conditional to marketing authorisation to standard marketing authorisation. Annex II and Package Leaflet are updated accordingly. The RMP (version 12.2) is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Abiraterone acetate - ZYTIGA (CAP) - PSUSA/00000015/201704

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Aclidinium, formoterol - BRIMICA GENUAIR (CAP); DUAKLIR GENUAIR (CAP) - PSUSA/00010307/201705

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alipogene tiparvovec - GLYBERA[10] - PSUSA/00010056/201704

Applicant: uniQure biopharma B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For information

6.1.4. Apixaban - ELIQUIS (CAP) - PSUSA/00000226/201705

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Bezlotoxumab - ZINPLAVA (CAP) - PSUSA/00010576/201704

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Catumaxomab - REMOVAB (CAP) - PSUSA/00000581/201704 (with RMP)

Applicant: Neovii Biotech GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Ceritinib - ZYKADIA (CAP) - PSUSA/00010372/201704

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

[10] Marketing authorisation for Glybera expired on 28 October 2017

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Cholera vaccine (inactivated, oral) - DUKORAL (CAP) - PSUSA/00000730/201704

Applicant: Valneva Sweden AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - PSUSA/00010449/201705

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Dalbavancin - XYDALBA (CAP) - PSUSA/00010350/201705

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Daratumumab - DARZALEX (CAP) - PSUSA/00010498/201705

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Darunavir, cobicistat - REZOLSTA (CAP) - PSUSA/00010315/201705

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Decitabine - DACOGEN (CAP) - PSUSA/00009118/201705

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Delamanid - DELTYBA (CAP) - PSUSA/00010213/201704

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Dihydroartemisinin, piperaquine tetraphosphate - EURARTESIM (CAP) - PSUSA/00001069/201704

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Edoxaban - LIXIANA (CAP); ROTEAS (CAP) - PSUSA/00010387/201704

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Empagliflozin, linagliptin - GLYXAMBI (CAP) - PSUSA/00010539/201705

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Etelcalcetide - PARSABIV (CAP) - PSUSA/00010533/201705

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Febuxostat - ADENURIC (CAP) - PSUSA/00001353/201704

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Fentanyl[11] - IONSYS (CAP) - PSUSA/00010453/201705

Applicant: Incline Therapeutics Europe Ltd

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Fesoterodine - TOVIAZ (CAP) - PSUSA/00001387/201704

Applicant: Pfizer Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP); REVINTY ELLIPTA (CAP) - PSUSA/00010099/201705

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Follitropin beta - FERTAVID (CAP); PUREGON (CAP) - PSUSA/00001465/201705

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[11] Transdermal system - centrally authorised product only

6.1.24. Fulvestrant - FASLODEX (CAP) - PSUSA/00001489/201704

Applicant: AstraZeneca UK Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Golimumab - SIMPONI (CAP) - PSUSA/00001560/201704

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Ibrutinib - IMBRUVICA (CAP) - PSUSA/00010301/201705

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Insulin glargine - ABASAGLAR (CAP); LANTUS (CAP); LUSDUNA (CAP); TOUJEO (CAP) - PSUSA/00001751/201704

Applicants: Eli Lilly Regional Operations GmbH (Abasaglar), Sanofi-Aventis Deutschland GmbH (Lantus, Toujeo), Merck Sharp & Dohme Limited (Lusduna)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Insulin lispro - HUMALOG (CAP); LIPROLOG (CAP) - PSUSA/00001755/201704

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Ixazomib - NINLARO (CAP) - PSUSA/00010535/201705

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Ketoconazole[12] - KETOCONAZOLE HRA (CAP) - PSUSA/00010316/201705

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Lidocaine, prilocaine[13] - FORTACIN (CAP) - PSUSA/00010110/201705

Applicant: Plethora Solutions Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Lumacaftor, ivacaftor - ORKAMBI (CAP) - PSUSA/00010455/201705

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Methylthioninium chloride - METHYLTHIONINIUM CHLORIDE PROVEBLUE (CAP) - PSUSA/00002029/201705

Applicant: Provepharm SAS

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Mitotane - LYSODREN (CAP) - PSUSA/00002075/201704

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Centrally authorised product only
[13] Centrally authorised product only

6.1.35. Necitumumab - PORTRAZZA (CAP) - PSUSA/00010471/201705

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Obinutuzumab - GAZYVARO (CAP) - PSUSA/00010279/201704

Applicant: Roche Registration Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Osimertinib - TAGRISSO (CAP) - PSUSA/00010472/201705

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Palbociclib - IBRANCE (CAP) - PSUSA/00010544/201705

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - PSUSA/00010501/201705

Applicant: AstraZeneca AB

PRAC Rapporteur: Daniela Philadelphy

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP); Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - PREPANDRIX (CAP) - PSUSA/00002281/201705

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Parecoxib - DYNASTAT (CAP) - PSUSA/00002314/201703

Applicant: Pfizer Limited

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Pixantrone - PIXUVRI (CAP) - PSUSA/00009261/201705

Applicant: CTI Life Sciences Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Propranolol[14] - HEMANGIOL (CAP) - PSUSA/00010250/201704

Applicant: Pierre Fabre Dermatologie

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Radium (^{223}Ra) dichloride - XOFIGO (CAP) - PSUSA/00010132/201705

Applicant: Bayer AG

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Ramucirumab - CYRAMZA (CAP) - PSUSA/00010323/201704

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[14] Centrally authorised product only

6.1.46. Shingles (herpes zoster) vaccine (live) - ZOSTAVAX (CAP) - PSUSA/00009289/201705

Applicant: MSD Vaccins

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Siltuximab - SYLVANT (CAP) - PSUSA/00010254/201704

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Simeprevir - OLYSIO (CAP) - PSUSA/00010255/201705

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Sunitinib - SUTENT (CAP) - PSUSA/00002833/201704

Applicant: Pfizer Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Susoctocog alfa - OBIZUR (CAP) - PSUSA/00010458/201705

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Tafamidis - VYNDAQEL (CAP) - PSUSA/00002842/201705

Applicant: Pfizer Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/201704

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Tenofovir alafenamide - VEMLIDY (CAP) - PSUSA/00010575/201705

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Tilmanocept - LYMPHOSEEK (CAP) - PSUSA/00010313/201705

Applicant: Norgine B.V.

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/201705

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Tolvaptan[15] - JINARC (CAP) - PSUSA/00010395/201705

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Indicated for adults with autosomal dominant polycystic kidney disease (ADPKD)

6.1.57. Tolvaptan[16] - SAMSCA (CAP) - PSUSA/00002994/201705

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. Trifluridine, tipiracil - LONSURF (CAP) - PSUSA/00010517/201704

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.59. Ulipristal acetate[17] - ELLAONE (CAP) - PSUSA/00003074/201705

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.60. Vedolizumab - ENTYVIO (CAP) - PSUSA/00010186/201705

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Amlodipine, telmisartan - TWYNSTA (CAP); NAP - PSUSA/00000180/201704

Applicants: Boehringer Ingelheim International GmbH (Twynsta), various

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[16] Indicated for adults with hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH)
[17] Female emergency contraceptive

6.2.2. Bortezomib - BORTEZOMIB ACCORD (CAP); BORTEZOMIB HOSPIRA (CAP); BORTEZOMIB SUN (CAP); VELCADE (CAP); NAP - PSUSA/00000424/201704

Applicants: Accord Healthcare Ltd (Bortezomib Accord), Janssen-Cilag International NV (Velcade), Hospira UK Limited (Bortezomib Hospira), Sun Pharmaceutical Industries Europe B.V. (Bortezomib Sun), various

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Cytarabine - DEPOCYTE (CAP); NAP - PSUSA/00000911/201703

Applicants: Pacira Ltd (DepoCyte), various

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Efavirenz - STOCRIN (CAP); SUSTIVA (CAP); NAP - PSUSA/00001200/201704

Applicants: Merck Sharp & Dohme Limited (Stocrin), Bristol-Myers Squibb Pharma EEIG (Sustiva), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Ivabradine - CORLENTOR (CAP); IVABRADINE ANPHARM (CAP); PROCORALAN (CAP); NAP - PSUSA/00001799/201704

Applicants: Anpharm Przedsiebiorstwo Farmaceutyczne S.A. (Ivabradine Anpharm), Les Laboratoires Servier (Corlentor, Procoralan), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Mycophenolate mofetil - CELLCEPT (CAP); MYCLAUSEN (CAP); MYCOPHENOLATE MOFETIL TEVA (CAP); MYFENAX (CAP), NAP mycophenolic acid (NAP) - PSUSA/00010550/201705

Applicants: Roche Registration Limited (CellCept), Passauer Pharma GmbH (Myclausen), Teva B.V. (Mycophenolate mofetil Teva, Myfenax), various

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.7. Somatropin - NUTROPINAQ (CAP); OMNITROPE (CAP); SOMATROPIN BIOPARTNERS[18]; NAP - PSUSA/00002772/201703

Applicants: Ipsen Pharma (NutropinAq), Sandoz GmbH (Omnitrope), BioPartners GmbH (Somatropin Biopartners), various

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.8. Telmisartan - KINZALMONO (CAP), MICARDIS (CAP), PRITOR (CAP); telmisartan, hydrochlorothiazide - KINZALKOMB (CAP), MICARDISPLUS (CAP), PRITORPLUS (CAP); NAP - PSUSA/00002882/201704

Applicants: Boehringer Ingelheim International GmbH (Micardis, MicardisPlus), Bayer Pharma AG (Kinzalkomb, Kinzalmono, Pritor, PritorPlus), various

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Aceclofenac (NAP) - PSUSA/00000022/201703

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Carvedilol (NAP) - PSUSA/00000575/201704

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Cefodizime (NAP) - PSUSA/00000595/201703

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

[18] Marketing authorisation for Somatropin Partners expired on 9 November 2017

Action: For adoption of recommendation to CMDh

6.3.4. Cefuroxime axetil (NAP) - PSUSA/00009099/201704

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Cefuroxime sodium[19] (NAP) - PSUSA/00000615/201704

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Chloroprocaine hydrochloride (NAP) - PSUSA/00010078/201703

Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Clarithromycin (NAP) - PSUSA/00000788/201704

Applicant(s): various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Deoxycholic acid (NAP) - PSUSA/00010525/201704

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[19] All routes of administration except intracameral use

6.3.9. Diphtheria, tetanus, pertussis (acellular, component) vaccine (adsorbed) (NAP); diphtheria, tetanus, pertussis (acellular, component) vaccine (adsorbed) reduced antigens contents (NAP) - PSUSA/00001125/201703

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Doxylamine (NAP) - PSUSA/00001174/201704

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Epoprostenol (NAP) - PSUSA/00001242/201703

Applicant(s): various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Estradiol (17-beta), trimegestone (NAP) - PSUSA/00001275/201703

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Estradiol, norethisterone (NAP) - PSUSA/00001278/201703

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Etoricoxib (NAP) - PSUSA/00001334/201703

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Fenspiride (NAP) - PSUSA/00001368/201704

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Gentamicin[20] (NAP) - PSUSA/00009159/201703

Applicant(s): various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Glucosamine (NAP) - PSUSA/00001539/201703

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Isotretinoin[21] (NAP) - PSUSA/00010488/201705

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Itraconazole (NAP) - PSUSA/00001798/201703

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[20] For systemic use only
[21] Oral formulations only

6.3.20. Ivabradine, metoprolol (NAP) - PSUSA/00010381/201704

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Ivermectin[22] (NAP) - PSUSA/00010376/201704

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Lanthanum (NAP) - PSUSA/00003175/201703

Applicant(s): various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Latanoprost[23] (NAP) - PSUSA/00001834/201704

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Lidocaine, prilocaine[24] (NAP) - PSUSA/00001867/201703

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Linezolid (NAP) - PSUSA/00001888/201704

Applicant(s): various

PRAC Lead: Julie Williams

[22] For topical use only
[23] Medicinal products with paediatric indication(s)
[24] Centrally authorised product(s) excluded

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Moclobemide (NAP) - PSUSA/00002079/201704

Applicant(s): various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Mupirocin (NAP) - PSUSA/00002096/201703

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Omeprazole (NAP) - PSUSA/00002215/201704

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Paracetamol[25] (NAP) - PSUSA/00002311/201705

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Piribedil (NAP) - PSUSA/00002436/201703

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[25] Intravenous (IV) formulation(s) only

6.3.31. Piroxicam (NAP) - PSUSA/00002438/201704

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.32. Porfimer (NAP) - PSUSA/00010332/201704

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.33. Pravastatin (NAP) - PSUSA/00002500/201703

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.34. Racecadotril (NAP) - PSUSA/00002602/201703

Applicant: various

PRAC Lead: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.35. Sertraline (NAP) - PSUSA/00002696/201703

Applicant(s): various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.36. Simvastatin (NAP) - PSUSA/00002709/201704

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.37. Tioconazole (NAP); tioconazole, hydrocortisone (NAP) - PSUSA/00010382/201704

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.38. Tretinoin[26] (NAP) - PSUSA/00003015/201703

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.39. Triptorelin (NAP) - PSUSA/00003048/201703

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.40. Urofollitropin (NAP) - PSUSA/00003082/201703

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.41. Vinorelbine (NAP) - PSUSA/00003124/201704

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[26] oral formulation(s) only

6.3.42. Zidovudine (NAP) - PSUSA/00003143/201703

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Anakinra - KINERET (CAP) - EMEA/H/C/000363/LEG 028.1

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Doris Stenver

Scope: MAH's response to LEG 028 [review on the feasibility of conducting a PASS in order to evaluate the risk of adverse cardiovascular events associated with long-term use of anakinra in patients with rheumatoid arthritis (RA) as requested in the conclusions of EMEA/H/C/PSUSA/00000209/201605 adopted by PRAC in December 2016] as per the request for supplementary information (RSI) adopted in June 2017

Action: For adoption of advice to CHMP

6.4.2. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/LEG 096

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Cumulative review of T lymphocyte decrease overall, CD4+ and CD8+ lymphocyte decrease using all relevant data sources (spontaneous reports, clinical trials, literature) split by indication, focussing on data in which rituximab was used as monotherapy. In addition, cumulative review on the incidence of progressive multifocal leukoencephalopathy (PML) in rituximab treated patients stratified by indication and clinical setting using all available information, including an in-depth review of all risk factors for PML in rituximab treated patients, a discussion on the need for PML risk stratification strategies and proposals for a risk stratification algorithm and risk minimisation measures depending on the risk level, as requested in the conclusions of PSUSA/00002652/201611 adopted in June 2017

Action: For adoption of advice to CHMP

6.4.3. Ticagrelor - BRILIQUE (CAP) - EMEA/H/C/001241/LEG 022

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a detailed review on the potential interaction of ticagrelor with morphine as requested in the conclusions of PSUSA/00002948/201612 adopted in July 2017

Action: For adoption of advice to CHMP

6.4.4. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/001241/LEG 019

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a cumulative review on the important potential risk 'drug induced liver injury', as requested in the conclusions of PSUSA/00009325/201702 adopted at the October 2017 PRAC meeting

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[27]

7.1.1. Direct acting antivirals (DAAV) indicated for the treatment of hepatitis C: Daclatasvir – DAKLINZA (CAP); dasabuvir - EXVIERA (CAP); elbasvir, grazoprevir – ZEPATIER (CAP); ledipasvir, sofosbuvir - HARVONI (CAP); ombitasvir, peritepreviir, ritonavir – VIEKIRAX (CAP); simeprevir - OLYSIO (CAP); sofosbuvir – SOVALDI (CAP); sofosbuvir, velpatasvir – EPCLUSA (CAP) - EMEA/H/N/PSP/J/0056.1

Applicant(s): AbbVie Limited (Exviera, Viekirax), Bristol-Myers Squibb Pharma EEIG (Daklinza), Gilead Sciences International Ltd (Epclusa, Harvoni, Sovaldi), Janssen-Cilag International NV (Olysio), Merck Sharp & Dohme Limited (Zepatier)

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to PSP/J/0056 [Joint PASS protocol for a prospective, non-interventional study evaluating the risk of early recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAAV) therapy compared to HCV-infected patients without previous DAA therapy during routine clinical care with previous successfully treated HCC, as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted at the September 2017 PRAC meeting

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

7.1.2. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSA/S/0016.2

Applicant: Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to PSA/S/0016.1 [amended protocol for study for study CC-5013-MDS-012: a post-authorisation, non-interventional, retrospective, drug-utilisation study to describe the pattern of use of lenalidomide in patients with myelodysplastic syndromes (MDS) as agreed in the conclusions of EMEA/H/C/PSA/S/0016 in April 2017] as per the request for supplementary information (RSI) adopted at the October 2017 PRAC meeting

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

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

7.1.3. Parathyroid hormone – NATPAR (CAP) - EMEA/H/C/PSP/S/0058.1

Applicant: Shire Pharmaceuticals Ireland

PRAC Rapporteur: Almath Spooner

Scope: MAH's response to PSP/S/0058 [PASS protocol for a registry for subjects with chronic hypoparathyroidism (PARADIGHM: physicians advancing disease knowledge in hypoparathyroidism)] as per the request for supplementary information adopted at the September 2017 PRAC meeting

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

7.1.4. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/PSA/S/0018.1

Applicant: Bayer AG

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's response to PSA/S/0018 [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)] as per the request for supplementary information adopted in July 2017

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[28]

7.2.1. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/MEA 050.1

Applicant: Teva B.V.

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to MEA 050 including a revised protocol [submission of a protocol for a post-authorisation long term safety cohort study in acute promyelocytic leukaemia (APL) patients treated with Trisenox (arsenic trioxide) to assess the long-term safety of all-trans retinoic acid (ATRA) + arsenic trioxide (ATO) in newly diagnosed low to intermediate risk APL patients in a real-world clinical practice setting as requested in the conclusions of variation II/0058 finalised in October 2016] as per the request for supplementary information (RSI) adopted in June 2017

Action: For adoption of advice to CHMP

[28] 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

7.2.2. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 003

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Protocol for an observational safety study using an existing database, study I4V-MC-B004: a retrospective cohort study to assess the long-term safety of baricitinib compared with other therapies used in the treatment of adults with moderate-to-severe rheumatoid arthritis in the course of routine clinical care [final report due date: 31/03/2031] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.3. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 004

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Protocol for assessing the effectiveness of the patient alert card and healthcare professional educational material, study I4V-MC-B010: a rheumatologist survey to assess the effectiveness of the risk minimisation measures (RMM) for Olumiant (baricitinib); and objective 3 of study I4V-MC-B011: a retrospective cohort study to assess the safety of baricitinib compared with other therapies used in the treatment of rheumatoid arthritis in Nordic countries [final report anticipated within 4 months following the end of data] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.4. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 005

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Protocol for an observational post marketing disease registry in EU patients, study I4V-MC-B011: a retrospective cohort study to assess the safety of baricitinib compared with other therapies used in the treatment of rheumatoid arthritis in Nordic countries (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.5. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 008

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Protocol for an observational post marketing disease registry in EU patients, study I4V-MC-B012: a post-marketing safety surveillance of baricitinib in three European registers (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.6. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 033.1

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 033 [protocol for study MK-8259-050: an observational PASS for golimumab in treatment of poly-articular juvenile idiopathic arthritis (pJIA) using the German Biologics JIA registry (BiKeR) as requested in the conclusions of variation procedure II/63] as per the request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

7.2.7. Insulin detemir - LEVEMIR (CAP) - EMEA/H/C/000528/MEA 045.7

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Doris Stenver

Scope: Submission of a substantial protocol amendment to the ongoing diabetes pregnancy registry (NN304-4016): an international non-interventional prospective cohort study to evaluate the safety of treatment with Levemir (insulin detemir) in pregnancy women with diabetes mellitus in order to reduce the total sample size [protocol previously adopted within procedure EMEA/H/C/000528/MEA 045.3 in May 2015]

Action: For adoption of advice to CHMP

7.2.8. Levetiracetam - KEPPRA (CAP) - EMEA/H/C/000277/MEA 086.2

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to MEA 086 [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)] as adopted in July 2017

Action: For adoption of advice to CHMP

7.2.9. Loxapine - ADASUVE (CAP) - EMEA/H/C/002400/MEA 001.3

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Sabine Straus

Scope: MAH's response to MEA 001.2 [revised protocols for: 1) study AMDC-204-401 (PASS): a post-authorisation observational study to evaluate the safety of Adasuve (loxapine for inhalation) in agitated persons in routine clinical care and study; 2) study 204-403 (drug utilisation study (DUS)): a multinational retrospective medical record to evaluate utilisation patterns of Adasuve (loxapine for inhalation) in agitated persons in routine clinical care] as per the request for supplementary information (RSI) adopted in June 2017

Action: For adoption of advice to CHMP

7.2.10. Olaratumab - LARTRUVO (CAP) - EMEA/H/C/004216/MEA 001.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sabine Straus

Scope: MAH's response to MEA 001 [protocol for study I5B-MC-B001: an observational PASS to evaluate the safety and effectiveness of olaratumab in combination with doxorubicin in patients with advanced soft tissue sarcoma (STS) including rare subtypes (as requested in the conclusions of the initial opinion/MA)] as per the request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

7.2.11. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 002

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Protocol for study A3921133 (RMP category 3): a phase 3B/4 randomised safety endpoint study of 2 doses of tofacitinib in comparison to a tumour necrosis factor (TNF) inhibitor in subjects with rheumatoid arthritis (RA) [final report due date: by 31 December 2020] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[29]

7.3.1. Pirfenidone – ESBRIET (CAP) - EMEA/H/C/PSR/S/0011

Applicant: Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Final study report for an imposed PASS: a prospective observational registry to evaluate the long-term safety of Esbriet (pirfenidone) in a real-world setting (passport)

Action: For adoption of recommendation to CMDh (or request for supplementary information (RSI))

7.4. Results of PASS non-imposed in the marketing authorisation(s)[30]

7.4.1. Aclidinium bromide - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/WS1207/0034; EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/WS1207/0034

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

[29] In accordance with Article 107p-q of Directive 2001/83/EC
[30] 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

Scope: Submission of the final report for study D6560R00005: a drug utilisation post-authorisation safety studies (DUS 1) in the United Kingdom, Denmark, and Germany listed as a category 3 study in the RMP (MEA002) aiming at describing the characteristics of new users of aclidinium bromide and of other chronic obstructive pulmonary disease (COPD) medications, evaluating the potential off-label use of aclidinium bromide in adults, pregnant women, and children, identifying and describing users of aclidinium bromide in patient subgroups for which there is missing information in the EU-RMP, and establishing a cohort of new users of aclidinium bromide for the future evaluation of safety concerns described in the RMP. The RMP (version 6.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0039

Applicant: Bayer AG

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of the final report for PASS study 16526 (RMP category 3 study): an observational study to evaluate the physician and patient knowledge of safety and safe use information for aflibercept in Europe as stated in the EU educational material of Eylea

Action: For adoption of PRAC Assessment Report

7.4.3. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/II/0048

Applicant: Bristol-Myers Squibb, Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report for study B0661073 (RMP category 4 study): a non-interventional PASS on the utilisation patterns of apixaban in Denmark. The RMP (version 18.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0047/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) submission of the final report for study IM103061 (RMP category 3 study): an epidemiological study on pregnancy outcome among belatacept users in the US; 2) submission of the final report for study IM103089 (RMP category 3 study): evaluation of retrospective data to assess the association between belatacept and the risk of post-transplant lymphoproliferative disorder (PTDL) in renal transplant recipients in Europe. The RMP (version 15) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS1229/0019, FORXIGA (CAP) - EMEA/H/C/002322/WS1229/0039 dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/WS1229/0025,

XIGDUO (CAP) - EMEA/H/C/002672/WS1229/0036

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final report from study D1690R00013. listed as a category 3 study in the RMP: incidence of diabetic ketoacidosis (DKA) among patients with type 2 diabetes (T2DM) in the United States. The RMPs (Forxiga, Edistride (version 15); Xigduo, Ebymect (version 10)) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS1259/0018, FORXIGA (CAP) - EMEA/H/C/002322/WS1259/0038 dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/WS1259/0024, XIGDUO (CAP) - EMEA/H/C/002672/WS1259/0035

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final report for a drug utilisation study (DUS) MB102-134, listed as a category 3 study in the RMP: an observational single-cohort data base study of dapagliflozin use in Europe. The RMPs (Forxiga, Edistride (version 15); Xigduo, Ebymect (version 10)) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. Duloxetine - ARICLAIM (CAP) - EMEA/H/C/000552/WS1264/0068, CYMBALTA (CAP) - EMEA/H/C/000572/WS1264/0072, DULOXETINE LILLY (CAP) - EMEA/H/C/004000/WS1264/0008, XERISTAR (CAP) - EMEA/H/C/000573/WS1264/0075, YENTREVE (CAP) - EMEA/H/C/000545/WS1264/0058

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final report from study F1J-MC-B056, listed as a category 3 study in the RMP: a non-interventional non-imposed study aimed to investigate the association between duloxetine exposure and suicide-related behaviours and ideation in women with stress urinary inconsistence (SUI). The RMP (version 12.3) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/II/0035/G

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Patrick Batty

Scope: Grouped variations consisting of an update of section 5.3 of the SmPC in order to revise the carcinogenicity information for idelalisib based on final results from two long term carcinogenicity studies: 1) study TX-312-2017: a 2-year oral (gavage) carcinogenicity study of idelalisib in sprague dawley rats; 2) study TX-312-2019: a 26-week oral gavage

carcinogenicity and toxicokinetic study with idelalisib in RasH2 [001178-T (hemizygous), CByB6F1-Tg(HRAS)2Jic] mice. The RMP (version 2.3) is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10.0)

Action: For adoption of PRAC Assessment Report

7.4.9. Interferon beta-1b - BETAFERON (CAP) - EMEA/H/C/000081/II/0118

Applicant: Bayer AG

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report from study BETAPAEDIC, listed as a category 3 study in the RMP: a non-interventional study evaluating safety and tolerability of Betaferon (interferon beta-1b) in paediatric patients with multiple sclerosis. The RMP (version 3.2) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.10. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/II/0055

Applicant: Bayer AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final study report for study 16171, a non-interventional PASS listed as a category 3 study in the RMP (MEA 019): an observational post-authorisation safety specialist cohort event monitoring study (SCEM) to monitor the safety and utilisation of rivaroxaban (Xarelto) for the prevention of stroke in patients with atrial fibrillation (AF), treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and the prevention of recurrent DVT and PE in the secondary care setting in England and Wales (ROSE study)

Action: For adoption of PRAC Assessment Report

7.4.11. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/WS1256/0059; Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS1256/0044

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report for study GS-EU-337-2030, listed as a category 3 study in the RMP: an observational, cross-sectional post-authorisation safety study to assess healthcare provider awareness of risks related to sofosbuvir and ledipasvir/sofosbuvir

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. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 046.7

Applicant: AbbVie Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Eight annual interim report for study P10-262, a registry study in juvenile idiopathic arthritis (JIA) patients: a long term, multicentre, longitudinal post-marketing, observational study to assess long term safety and effectiveness of Humira (adalimumab) in children with moderately to severely active polyarticular or polyarticular-course JIA – STRIVE [final study report due date: 31 December 2024] (from variation II/39)

Action: For adoption of advice to CHMP

7.5.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 075.6

Applicant: AbbVie Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fifth annual interim study report for Humira ulcerative colitis registry P11-282: a long-term non-interventional postmarketing study to assess safety and effectiveness of Humira (adalimumab) in patients with moderately to severely active ulcerative colitis (UC)

Action: For adoption of advice to CHMP

7.5.3. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 080.5

Applicant: AbbVie Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Third annual interim report for P11-292 registry: a long-term non-interventional registry to assess safety and effectiveness of Humira (adalimumab) in paediatric patients with moderately to severely active Crohn’s disease (CD) CAPE

Action: For adoption of advice to CHMP

7.5.4. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/MEA 023

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study BMS IM103-074: a retrospective analysis of data from the United Network for Organ Sharing (UNOS) to describe the pattern of Nulojix (belatacept) use at the time of transplant pregnancy outcome among belatacept users in the US

Action: For adoption of advice to CHMP

7.5.5. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/MEA 024

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study BMS IM103-075: a retrospective analysis of data from the United Network for Organ Sharing (UNOS) to assess the association between Nulojix (belatacept) use and risk of post-transplant lymphoproliferative disorder (PTLD) in renal transplant recipients in the US

Action: For adoption of advice to CHMP

7.5.6. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/MEA 025

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study BMS IM103076: a prospective registry study evaluating Nulojix (belatacept) long-term safety in transplant (ENLIST) to describe the pattern of Nulojix (belatacept) use at the time of transplant

Action: For adoption of advice to CHMP

7.5.7. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/MEA 026

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study BMS IM103077: a retrospective analysis of data from collaborative transplant study (CTS) to describe the pattern of Nulojix (belatacept) use at the time of transplant

Action: For adoption of advice to CHMP

7.5.8. Colistimethate sodium - COLOBREATHE (CAP) - EMEA/H/C/001225/MEA 013

Applicant: Teva B.V.

PRAC Rapporteur: Julie Williams

Scope: Second to sixth interim reports for study CLB-MD-05: an open-label observational safety study of Colobreathe (colistimethate sodium dry powder for inhalation) compared with other inhaled antipseudomonal antibiotics in cystic fibrosis patients using cystic fibrosis registries

Action: For adoption of advice to CHMP

7.5.9. Golimumab – SIMPONI (CAP) - EMEA/H/C/000992/MEA 007.2

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Third annual report from a pregnancy research initiative to study the exposure to golimumab during pregnancy in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers (CNTO148ART4001)

Action: For adoption of advice to CHMP

7.5.10. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/MEA 028.5

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Fifth interim report of a PASS study, listed as a category 3 study in the RMP: a post-approval safety surveillance for monthly lot-specific adverse event review and analysis to evaluate any potential change in the frequency of hypersensitivity and immunogenicity events with the altered manufacturing process (sKPB) of Humalog and Liprolog. This fourth interim report covers the batches released to the market between 15 October 2013 and 31 January 2017

Action: For adoption of advice to CHMP

7.5.11. Insulin lispro - LIPROLOG (CAP) - EMEA/H/C/000393/MEA 021.5

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Fifth interim report of a PASS study, listed as a category 3 study in the RMP: a post-approval safety surveillance for monthly lot-specific adverse event review and analysis to evaluate any potential change in the frequency of hypersensitivity and immunogenicity events with the altered manufacturing process (sKPB) of Humalog and Liprolog. This fourth interim report covers the batches released to the market between 15 October 2013 and 31 January 2017

Action: For adoption of advice to CHMP

7.5.12. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/MEA 008.3

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Interim report for study CA209234, listed as a category 3 in the RMP: a PASS exploring the pattern of use, safety, and effectiveness of Nivolumab in routine oncology practice [final clinical study report (CSR) due date: 31 December 2024] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.5.13. Sapropterin - KUVAN (CAP) - EMEA/H/C/000943/MEA 003.7

Applicant: BioMarin International Limited

PRAC Rapporteur: Almath Spooner

Scope: Seventh annual interim report for the Kamper registry, study EMR700773-001: a non-imposed, non-interventional exploring the long-term safety of Kuvan (sapropterin) use in patients with hyperphenylalaninaemia (HPA) as well as information regarding Kuvan use during pregnancy in women with HPA and data regarding childhood growth and neurocognitive outcomes

Action: For adoption of advice to CHMP

7.5.14. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/MEA 004.1

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice [final report due date: planned for 2020]

Action: For adoption of advice to CHMP

7.5.15. Simoctocog alfa - VIHUMA (CAP) - EMEA/H/C/004459/MEA 004

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice [final report due date: planned for 2020]

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Rituximab - RIXATHON (CAP) - EMEA/H/C/003903/MEA 004

Applicant: Sandoz GmbH

PRAC Rapporteur: Doris Stenver

Scope: Interim report for study GP13-302, listed as a category 3 study in the RMP: a randomized, double-blind, controlled, parallel-group, multicentre study to assess the safety and immunogenicity of transitioning to GP2013 (Rixathon/Riximyo (biosimilar rituximab)) or retreatment with Rituxan/MabThera (rituximab) in patients with active rheumatoid arthritis, previously treated with Rituxan/MabThera. (12 week interim report: after EC decision) (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.6.2. Rituximab - RIXIMYO (CAP) - EMEA/H/C/004729/MEA 004

Applicant: Sandoz GmbH

PRAC Rapporteur: Doris Stenver

Scope: Interim report for study GP13-302, listed as a category 3 study in the RMP: a randomized, double-blind, controlled, parallel-group, multicentre study to assess the safety and immunogenicity of transitioning to GP2013 (Rixathon/Riximyo (biosimilar rituximab)) or retreatment with Rituxan/MabThera (rituximab) in patients with active rheumatoid arthritis, previously treated with Rituxan/MabThera. (12 week interim report: after EC decision) (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

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

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Antithrombin alfa - ATRYN (CAP) - EMEA/H/C/000587/S/0030 (without RMP)

Applicant: GTC Biotherapeutics UK Limited

PRAC Rapporteur: Caroline Laborde

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/003794/S/0024 (without RMP)

Applicant: Alexion Europe SAS

PRAC Rapporteur: Almath Spooner

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 marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/R/0027 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/R/0027 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Avanafil - SPEDRA (CAP) - EMEA/H/C/002581/R/0029 (without RMP)

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - EMEA/H/C/002574/R/0086 (with RMP)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/R/0037 (without RMP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Memantine - MEMANTINE RATIOPHARM (CAP) - EMEA/H/C/002671/R/0011 (without RMP)

Applicant: ratiopharm GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Micafungin - MYCAMINE (CAP) - EMEA/H/C/000734/R/0034 (without RMP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/R/0042 (without RMP)

Applicant: Incyte Biosciences UK Ltd

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Thalidomide - THALIDOMIDE CELGENE (CAP) - EMEA/H/C/000823/R/0054 (without RMP)

Applicant: Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Voriconazole - VORICONAZOLE ACCORD (CAP) - EMEA/H/C/002669/R/0017 (without RMP)

Applicant: Accord Healthcare Limited

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

9.1.1. Risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders connected with human centrally authorised products

Scope: Pharmacovigilance inspection programme 2017-2020 (second revision for 2017)

Action: For adoption

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/II/0038

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Patrick Batty; PRAC Co-rapporteur: Ulla Wändel Liminga

Scope: CHMP request for PRAC advice on a variation to update sections 4.2, 4.4 and 4.8 of the SmPC in order to reflect information from a recent cumulative safety review of cases of organising pneumonia. The Package Leaflet and Labelling are updated accordingly. The RMP (version 2.6) is also updated to extend the deadlines for submission of final clinical study report (CSR) for three studies linked to Annex II conditions

Action: For adoption of advice to CHMP

See also under 5.3.20.

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

None

10.3. Other requests

None

10.4. Scientific Advice

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. Lenalidomide - DK/H/2772-2773, 2775, NL/H/4067-68/001-007/DC, DE/H/5336/01-07/DC, NL/H/4082/001-7/DC

PRAC Lead: Martin Huber

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

None

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 adoption

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

12.3.1. Scientific advice working party (SAWP) – re-nomination of PRAC representative(s)

Action: For adoption

12.4. Cooperation within the EU regulatory network

12.4.1. Brexit: preparedness of the regulatory network and capacity increase

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 2018 – preparation

PRAC lead: June Raine, Almath Spooner

Action: For discussion

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, 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. Signal management – feedback from Signal Management Review Technical (SMART) Working Group

PRAC lead: Sabine Straus

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality - EudraVigilance auditable requirement project – update and next steps

Action: For discussion

12.13.2. Activities related to the confirmation of full functionality - EudraVigilance auditable requirement project – new functionalities

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

12.17. 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. Committees/EMA external representation - user manual

Action: For discussion

12.20.2. Strategy on measuring the impact of pharmacovigilance – revised strategy and work plan 2018

PRAC lead: Marieke de Bruin

Action: For adoption

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/