25 September 2017
EMA/PRAC/634126/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 25-29 September 2017

Chair: June Raine – Vice-Chair: Almath Spooner

25 September 2017, 13:00 – 19:30, room 3/A

26 September 2017, 08:30 – 19:30, room 3/A

27 September 2017, 08:30 – 19:30, room 3/A

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

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

Organisational, regulatory and methodological matters (ORGAM) 12 October 2017, 09:00-12:00, room 7/B, via Adobe Connect

Health and safety information

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

Disclaimers

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

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

Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006, Rev. 1).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
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Table of contents

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held on 25-29 September 2017. See October 2017 PRAC minutes (to be published post November 2017 PRAC meeting).

1.2. Agenda of the meeting on 25-29 September 2017

Action: For adoption

1.3. Minutes of the previous meeting on 29 August-1 September 2017

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

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

Applicant(s): Biogen Idec Ltd

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

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

Action: For adoption of the list of experts (LoE) for the Scientific advisory group (SAG) on neurology meeting

3.2.2. Fluoroquinolones for systemic and inhalation use: ciprofloxacin (NAP); enoxacin (NAP); flumequin (NAP); levofloxacin – QUINSAIR (CAP), NAP; lomefloxacin (NAP); moxifloxacin (NAP); norfloxacin (NAP); ofloxacin (NAP); pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP) Quinolones for systemic and inhalation use: cinoxacin (NAP); nalidixic acid (NAP); pipemidic acid (NAP) - EMEA/H/A-31/1452

Applicant(s): Raptor Pharmaceuticals Europe BV (Quinsair), various

PRAC Rapporteur: Eva Jirsová; PRAC Co-rapporteur: Martin Huber

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

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

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

Applicant(s): Sanofi-aventis, various

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

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

Action: For holding a public hearing and for adoption of the lists of experts (LoE) for the Scientific advisory group (SAG) on neurology, SAG on psychiatry and stakeholders meetings

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

3.4.1. Paracetamol[2] (NAP); paracetamol, tramadol[2] (NAP) - EMEA/H/A-31/1445

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

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

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

Action: For discussion

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Apixaban – ELIQUIS (CAP); dabigatran – PRADAXA (CAP); edoxaban – LIXIANA (CAP); rivaroxaban – XARELTO (CAP)

Applicant(s): Bayer AG (Xarelto), Boehringer Ingelheim International GmbH (Pradaxa); Bristol-Myers Squibb- Pfizer EEIG (Eliquis); Daiichi Sankyo Europe GmbH (Lixiana)

PRAC Rapporteur: To be appointed

Scope: Signal of cholesterol embolisms

Action: For adoption of PRAC recommendation

EPITT 19078 – New signal

Lead Member State(s): NL, SE, DK, UK

4.1.2. Baricitinib – OLUMIANT (CAP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Signal of pneumonia

[1] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[2] Modified release formulations only
[3] Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

Action: For adoption of PRAC recommendation

EPITT 18950 – New signal

Lead Member State: UK

4.1.3. Exenatide – BYDUREON (CAP), BYETTA (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of cardiac arrhythmias

Action: For adoption of PRAC recommendation

EPITT 18938 – New signal

Lead Member State: SE

4.1.4. Iloprost – VENTAVIS (CAP)

Applicant: Bayer Pharma AG

PRAC Rapporteur: Caroline Laborde

Scope: Signal of bradycardia

Action: For adoption of PRAC recommendation

EPITT 18935 – New signal

Lead Member State: FR

4.1.5. Teriflunomide – AUBAGIO (CAP)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Signal of lymphoma

Action: For adoption of PRAC recommendation

EPITT 18960 – New signal

Lead Member State: DE

4.2. New signals detected from other sources

4.2.1. Gonadotropin-releasing hormone (GnRH) agonists: Buserelin (NAP); goserelin (NAP); leuprorelin (NAP); triptorelin (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of thromboembolic events

Action: For adoption of PRAC recommendation

EPITT 19084 – New signal

Lead Member State(s): DE, IT, SE

4.3. Signals follow-up and prioritisation

4.3.1. Acetazolamide (NAP)

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of acute generalised exanthematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 18892 - Follow-up to May 2017

4.3.2. Azithromycin (NAP); clarithromycin (NAP); erythromycin (NAP); roxithromycin (NAP)

Applicant(s): various

PRAC Rapporteur: Almath Spooner

Scope: Signal of acute generalised exanthematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 18891 - Follow-up to May 2017

4.3.3. Cladribine - LITAK (CAP) - EMEA/H/C/000504/SDA/025; NAP

Applicant(s): Lipomed GmbH, various

PRAC Rapporteur: Patrick Batty

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

Action: For adoption of PRAC recommendation

EPITT 18875 – Follow-up to May 2017

4.3.4. Desloratadine – AERINAZE (CAP) – EMEA/H/C/000772/SDA/016, AERIUS (CAP) - EMEA/H/C/000313/SDA/067, AZOMYR (CAP) - EMEA/H/C/000310/SDA/067, DASSELTA (CAP) - EMEA/H/C/002310/SDA/003, DESLORATADINE ACTAVIS (CAP) - EMEA/H/C/002435/SDA/003, DESLORATADINE RATIOPHARM (CAP) - EMEA/H/C/002404/SDA/003, DESLORATADINE TEVA (CAP) - EMEA/H/C/002419/SDA/003, NEOCLARITYN (CAP) - EMEA/H/C/000314/SDA/067; loratadine (NAP)

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

PRAC Rapporteur: Laurence de Fays

Scope: Signal of weight increase in children

Action: For adoption of PRAC recommendation

EPITT 18906 – Follow-up to July 2017

4.3.5. Doxycycline (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal of doxycycline induced Jarisch-Herxheimer reaction

Action: For adoption of PRAC recommendation

EPITT 18937 – Follow-up to September 2017

4.3.6. Flucloxacillin (NAP)

Applicant(s): various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Signal of high anion gap metabolic acidosis (HAGMA)

Action: For adoption of PRAC recommendation

EPITT 18844 – Follow-up to April 2017

4.3.7. Gefitinib - IRESSA (CAP) - EMEA/H/C/001016/SDA/024

Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of recall phenomenon

Action: For adoption of PRAC recommendation

EPITT 18857 – Follow-up to April 2017

4.3.8. Insulin[4]:

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) -

[4] Pre-filled pens and cartridges

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 May 2017

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Betrixaban - EMEA/H/C/004309

Scope: Treatment of prophylaxis of venous thromboembolism (VTE)

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

5.1.2. Brigatinib - EMEA/H/C/004248

Scope: Treatment of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC)

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

5.1.3. Burosumab - EMEA/H/C/004275, Orphan

Applicant: Kyowa Kirin Limited

Scope: Treatment of X-linked hypophosphataemia (XLH)

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

5.1.4. Emicizumab - EMEA/H/C/004406

Scope, accelerated assessment: Treatment and routine prophylaxis to prevent bleeding or reduce the frequency of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors

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

5.1.5. Enclomifene - EMEA/H/C/004198

Scope: Treatment of hypogonadotrophic hypogonadism

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

5.1.6. Hydrocortisone - EMEA/H/C/004416, PUMA[5]

Scope: Treatment of adrenal insufficiency

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

5.1.7. Insulin glargine - EMEA/H/C/004280

Scope: Treatment of diabetes mellitus

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

5.1.8. Masitinib - EMEA/H/C/004398, Orphan

Applicant: AB Science

Scope: Treatment of amyotrophic lateral sclerosis

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

5.1.9. Peramivir - EMEA/H/C/004299

Scope: Treatment of influenza

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: Update of the 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

[5] Paediatric-use marketing authorisation(s)

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. Miglustat - ZAVESCA (CAP) - EMEA/H/C/000435/II/0057, Orphan

Applicant: Actelion Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP (version 12.2) in order to remove important identified risks such as diarrhoea and other gastrointestinal (GI) events and tremor as well as important potential risks such as seizure in Niemann-Pick type C (NP-C) patients

Action: For adoption of PRAC Assessment Report

5.2.3. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[6]) - EMEA/H/W/002300/II/0020

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of the RMP (version 3.0) in order to 1) add cerebral malaria as an important potential risk; 2) add mortality by gender as missing information; 3) add the WHO[7] pilot implementation programme as a category 3 study; 4) change the study dates for studies malaria-073 (200596, phase IIIb randomized, open, controlled study to evaluate the immunogenicity and safety of Mosquirix, when administered as primary vaccination at 6, 7.5 and 9 months of age with or without coadministration of measles and rubella and yellow fever vaccines to children living in sub-Saharan, Africa), EPI-MAL-002 (115055, an observational cohort study to estimate the incidence of adverse event of special interest (AESI), of meningitis and of other adverse events (AE) leading to hospitalisation or death, in children, prior to implementation of Mosquirix), EPI-MAL-003 (115056, a prospective surveillance study to evaluate the safety, the effectiveness and the impact of Mosquirix in infants and young children in sub-Saharan Africa), EPI-MAL-005 (116682, an epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post-Mosquirix introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit-risk in children in sub-Saharan Africa), EPI-MAL-010 (205071, a longitudinal, cross-sectional ancillary study of the EPI-MAL-005 study to evaluate the genetic diversity in circumsporozoite sequences before and after the implementation of Mosquirix in malaria-positive subjects ranging from 6 months to less than 5 years of age); 5) amend the protocol of study EPI-MAL-002; 6) update the draft protocol of study EPI-MAL-003; 7) provide a new draft of the protocol of study EPI-MAL-010, 8) provide a new protocol for the pilot implementation programme

Action: For adoption of PRAC Assessment Report

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

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

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Action: For adoption of PRAC Assessment Report

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

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

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer and in combination with androgen deprivation therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 14.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

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

5.3.2. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/II/0001

Applicant: Roche Registration Limited

PRAC Rapporteur: Patrick Batty

Scope: Extension of indication to first line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC). As a consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 2.0) are updated accordingly

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

5.3.3. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/II/0017

Applicant: Celgene Europe Limited

PRAC Rapporteur: Eva Segovia

Scope: Update of section 4.4 of the SmPC to include a warning on serious diarrhoea, nausea, and vomiting following a safety cumulative review of all data sources. The Package

Leaflet is updated accordingly. In addition, the RMP (version 9.0) is updated to classify serious diarrhoea, nausea, and vomiting as important potential risks. The MAH took the opportunity to introduce editorial changes in Annex IIIA and to bring the Product Information in line with the latest QRD template (version 10.0)

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

5.3.4. Atazanavir,cobicistat - EVOTAZ (CAP) - EMEA/H/C/003904/WS1193/0018; Atazanavir, atazanavir sulfate - REYATAZ (CAP) - EMEA/H/C/000494/WS1193/0113

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Caroline Laborde

Scope: Update of sections 4.3 and 4.5 of the SmPC to include information on the contraindicated co-administration with grazoprevir-containing products, including elbasvir/grazoprevir fixed dose combination used for the treatment of chronic hepatitis C infection following the results of interaction studies. The Package Leaflets and the RMPs (Evotaz (version 5.0), Reyataz (version 13.0)) are updated accordingly. In addition, the MAH took the opportunity to make some editorial changes and typographical corrections in the Reyataz and Evotaz Product Information

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

5.3.5. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0018, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include children aged one month and older to the authorised population for the treatment of adults with Philadelphia chromosome-negative relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated in order to include the new population, update the posology and the safety information. The Package Leaflet and the RMP (version 6.0) are updated accordingly

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

5.3.6. Brivaracetam - BRIVIACT (CAP) - EMEA/H/C/003898/II/0010/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped application consisting of 1) extension of indication to include adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy 4 years of age and older. As a consequence, sections 4.1, 4.2, 4.7, 5.1 and 5.2 of the SmPC are updated; 2) submission of a 5ml oral syringe and adaptor for the paediatric population. The Package Leaflet, Labelling and the RMP (version 6.1) are updated accordingly. The submission also includes a final environmental risk assessment (ERA) for the inclusion of the paediatric population in accordance with the new proposed indication

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

5.3.7. 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

5.3.8. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0015

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4, 4.5, 4.8 and 5.2 of the SmPC in order to update the safety information based on the primary pharmacokinetic (PK) and preliminary safety results of food effect study CLDK378A2112: a multicentre, randomized open label study to assess the systemic exposure, efficacy, and safety of 450 mg ceritinib taken with a low-fat meal and 600 mg ceritinib taken with a low-fat meal as compared with that of 750 mg ceritinib taken in the fasted state in adult patients with anaplastic lymphoma kinase (ALK) rearranged (ALK-positive) metastatic non-small cell lung cancer (NSCLC). 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

5.3.9. 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. Daptomycin - CUBICIN (CAP) - EMEA/H/C/000637/II/0061

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to extend the *S. aureus* bacteraemia indication to include paediatric patients 1 to 17 years of age. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet, Labelling and the RMP (version 10.0) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10) and to combine the SmPCs for both strengths (350 and 500 mg)

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

5.3.11. 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

5.3.12. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0056

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to modify the special warnings and precautions for use and undesirable effects sections following the performance of a cumulative safety review of multiple vertebral fractures (MVF) following treatment discontinuation based on two clinical trials: study 20060359: an ongoing randomized, placebo-controlled, blinded study of denosumab as adjuvant treatment for women with early-stage breast cancer at high risk of recurrence and study 20040113: a completed phase 2 study comparing denosumab and intravenous (IV) bisphosphonate treatment, collected data on bone turnover markers during the 32-week post-treatment follow-up period as well as based on post-marketing experience data. The Package Leaflet and the RMP (version 26.0) are updated accordingly. A direct healthcare professional communication (DHPC) is also proposed to inform prescribers about the new identified risk of MVF following discontinuation of Xgeva

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

5.3.13. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0036/G

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Grouped variation consisting of: 1) submission of a clinical study report (CSR) for study 109HV321: a randomized, double-blind, phase 3b study to evaluate the safety and tolerability of BG00012 (dimethyl fumarate) when administered as 240 mg BID (twice daily) dose regimen with and without aspirin compared to placebo or following a slow titration (category 3); 2) submission of a CSR for study 109MS406 (ASSURE): a phase 4, randomized, double-blind study with a safety extension period to evaluate the effect of aspirin on flushing events in subjects with relapsing-remitting multiple sclerosis treated with Tecfidera (dimethyl fumarate) delayed-release capsules (category 4). The RMP (version 9.0) is updated accordingly

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

5.3.14. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0037

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Submission of a clinical study report (CSR) for study 109MS307: an open-label study to assess the immune response to vaccination in Tecfidera-treated versus interferon-treated subjects with relapsing forms of multiple sclerosis (category 3). As a consequence, section 4.5 of the SmPC is updated. 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

5.3.15. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/WS1190/0210/G; LIFMIOR (CAP) - EMEA/H/C/004167/WS1190/0009/G

Applicant: Pfizer Limited

PRAC Rapporteur: Patrick Batty

Scope: Grouped worksharing quality variation. An addendum to the RMP (version 6.3) is submitted accordingly

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

5.3.16. 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

5.3.17. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0033/G, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 5.1 of the SmPC in order to update the safety information related to bleeding related events based on final results from study PCYC-1132-NT (RMP, category 3 (MEA 004.1) study): an in-vitro study to evaluate the effect of ibrutinib on platelet aggregation. The Package Leaflet is updated accordingly; 2) update of section 4.4 and 4.5 of the SmPC in order to update the safety information based on the final results from study LYM1003 (RMP, category 3 (MEA 009.1) study): a drug-drug interaction study to assess steady state pharmacokinetic (PK) of repeated oral doses of ibrutinib alone in patients with B-cell malignancies and when combined with a moderate and strong CYP3A[8] inhibitor. The Package Leaflet is updated accordingly; 3) update of section 4.5 of the SmPC in order to update the safety information based on the final results from study FK12024: a drug-drug interaction (DDI) study with CYP3A inhibitor posaconazole in simulated subjects. The Package Leaflet is updated accordingly; 4) update of section 4.4 of the SmPC in order to update the safety information on antimicrobial prophylaxis following routine pharmacovigilance activity; 5) update of the RMP in order to extend the closure date of study PCYC-1112-CA (ANX 003.2: a randomized, multicentre, open-label, phase 3 study of the Bruton's tyrosine kinase (BTK) inhibitor ibrutinib (PCI-32765) versus ofatumumab in patients with relapsed or refractory chronic lymphocytic leukaemia/small lymphocytic lymphoma) to Q2 2019. Next yearly update will be submitted in Q2 2018. Annex II has been updated accordingly; 6) update of the RMP to include an additional action for study PCI-32765 CAN3001 (MEA017) to provide a 'further interim report in 5 years' from the time of the cut-off date of the current report (12 November 2015)' as agreed in the CHMP outcome for procedure EMA/H/C/003791/MEA 017. The RMP (version 6.8) is 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. Insulin degludec - TRESIBA (CAP) - EMEA/H/C/002498/II/0028

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 5.1 of the SmPC based on new clinical data from a cardiovascular outcome trial EX1250-4080 (DEVOTE): a randomised, double-blind and event-driven clinical study with a median duration of 2 years comparing the cardiovascular safety of Tresiba (insulin degludec) versus insulin glargine (100 units/mL) in patients with type 2 diabetes mellitus (T2DM) at high risk of cardiovascular events. The RMP (version 8) is updated accordingly

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

[8] Cytochrome P450, family 3, subfamily A

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

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

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

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

5.3.20. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/II/0017

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data from study VX12 809 105: a phase 3, rollover study to evaluate the safety and efficacy of long term treatment with lumacaftor/ivacaftor in subjects aged 12 years and older with cystic fibrosis, homozygous or heterozygous for the F508del cystic fibrosis transmembrane conductance regulator (CFTR) mutation (MEA 001). The RMP (version 2.7) 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

5.3.21. Migalastat - GALAFOLD (CAP) - EMEA/H/C/004059/II/0011, Orphan

Applicant: Amicus Therapeutics UK Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 4.2 of the SmPC to provide further information on missing doses and to improve the wording on the administration of migalastat with food. No new data is submitted to support these changes. In addition, the MAH took this opportunity to include the ATC[9] code and to update the local representatives in the package leaflet. As a consequence, changes are introduced in Annexes I, IIIA and IIIB. The RMP (version 2.0) is updated accordingly

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

5.3.22. 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

[9] Anatomical therapeutic chemical

CHMP

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

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Patrick Batty

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

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

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

Applicant: Roche Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to include paediatric patients from 3 to less than 18 years of age with chronic hepatitis B in the immune-active phase for Pegasys. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add efficacy and safety information from study YV25718: a phase 3b parallel group, open label study of pegylated interferon alfa-2a monotherapy compared to untreated control in children with HBeAg positive chronic hepatitis B. The Package Leaflet and the RMP (version 8.0) are updated accordingly

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

5.3.25. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/II/0039/G, Orphan

Applicant: Incyte Biosciences UK Ltd

PRAC Rapporteur: Patrick Batty

Scope: Grouped variations consisting of the submission of the final reports from two nonclinical studies performed to investigate the potential mechanism of action of ponatinib leading to vascular occlusion, namely 1) study RPT-03346: evaluation of the effects of ponatinib on arterial remodeling and wall thickening in a murine model of stenosis; 2) study RPT-03342: investigation of the effects of ponatinib on photochemical-induced thrombosis in mice and rats, conducted to further explore the potential relationship between ponatinib and thrombosis in a photochemical induced thrombosis model in mice and rats. The RMP (version 18) is updated accordingly

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

5.3.26. 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

5.3.27. Vemurafenib - ZELBORAF (CAP) - EMEA/H/C/002409/II/0042/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variation consisting of the submission of the final reports for: 1) study MO25515 (MEA006): an open-label multicentre study to assess the safety of RO5185426 (vemurafenib) in patients with metastatic melanoma; 2) study GP28492 (ZeSS) (MEA010): a prospective observational safety study of patients with BRAFV600 mutation positive unresectable or metastatic melanoma treated with vemurafenib. The RMP (version 10.3) is updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Albiglutide - EPERZAN (CAP) - PSUSA/00010175/201703

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alemtuzumab - LEMTRADA (CAP) - PSUSA/00010055/201703

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - ZALMOXIS (CAP) - PSUSA/00010530/201702

Applicant: MolMed SpA, ATMP[10]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Anidulafungin - ECALTA (CAP) - PSUSA/00000215/201701

Applicant: Pfizer Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Apremilast - OTEZLA (CAP) - PSUSA/00010338/201703

Applicant: Celgene Europe Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Bedaquiline - SIRTURO (CAP) - PSUSA/00010074/201703

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Belimumab - BENLYSTA (CAP) - PSUSA/00009075/201703

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[10] Advanced therapy medicinal product

6.1.8. Betaine anhydrous[11] - CYSTADANE (CAP) - PSUSA/00000390/201702 (with RMP)

Applicant: Orphan Europe SARL

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Bevacizumab - AVASTIN (CAP) - PSUSA/00000403/201702

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Bosutinib - BOSULIF (CAP) - PSUSA/00010073/201703

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Brentuximab vedotin - ADCETRIS (CAP) - PSUSA/00010039/201702

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Ceftazidime, avibactam - ZAVICEFTA (CAP) - PSUSA/00010513/201702

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Ceftolozane, tazobactam - ZERBAXA (CAP) - PSUSA/00010411/201703

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Adam Przybylkowski

[11] Centrally authorised product only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Cholic acid[12] - KOLBAM (CAP) - PSUSA/00010182/201703

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Ciclosporin[13] - IKERVIS (CAP) - PSUSA/00010362/201703

Applicant: Santen Oy

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Cobimetinib - COTELLIC (CAP) - PSUSA/00010450/201702

Applicant: Roche Registration Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Collagenase clostridium histolyticum[14] - XIAPEX (CAP) - PSUSA/00000871/201702

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dabigatran - PRADAXA (CAP) - PSUSA/00000918/201703

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Treatment of inborn errors in primary bile acid synthesis due to sterol 27-hydroxylase (presenting as cerebrotendinous xanthomatosis, CTX) deficiency, 2- (or α-) methylacyl-CoA racemase (AMACR) deficiency or cholesterol 7α-hydroxylase (CYP7A1) deficiency indications only

[13] Topical use only

[14] Treatment of Dupuytren's contracture and treatment of Peyronie's disease only

6.1.19. Dexamethasone[15] - NEOFORDEX (CAP) - PSUSA/00010480/201703

Applicant: Laboratoires CTRS

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Dexmedetomidine - DEXDOR (CAP) - PSUSA/00000998/201703 (with RMP)

Applicant: Orion Corporation

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated), haemophilus type b conjugate vaccine (adsorbed) - VAXELIS (CAP) - PSUSA/00010469/201702

Applicant: MCM Vaccine B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Dulaglutide - TRULICITY (CAP) - PSUSA/00010311/201703

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Eftrenonacog alfa - ALPROLIX (CAP) - PSUSA/00010499/201703

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Eliglustat - CERDELGA (CAP) - PSUSA/00010351/201702

Applicant: Genzyme Europe BV

[15] Centrally authorised product indicated in symptomatic multiple myeloma only

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Eluxadoline - TRUBERZI (CAP) - PSUSA/00010528/201703

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Emtricitabine, rilpivirine, tenofovir alafenamide - ODEFSEY (CAP) - PSUSA/00010514/201702

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Enoxaparin[16] - INHIXA (CAP), THORINANE (CAP) - PSUSA/00010553/201703

Applicants: Pharmathen S.A. (Thorinane), Techdow Europe AB (Inhixa)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Epoetin beta - NEORECORMON (CAP) - PSUSA/00001239/201702

Applicant: Roche Registration Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/201702

Applicant: Chiesi Farmaceutici S.p.A., ATMP[17]

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

[16] Biosimilars only
[17] Advanced therapy medicinal product

Action: For adoption of recommendation to CHMP

6.1.30. Fenofibrate, simvastatin - CHOLIB (CAP) - PSUSA/00010096/201702

Applicant: Mylan Products Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/201702

Applicant: Shield TX (UK) Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Fingolimod - GILENYA (CAP) - PSUSA/00001393/201702

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Fluticasone propionate, salmeterol[18] - AERIVIO SPIROMAX (CAP), AIREXAR SPIROMAX (CAP) - PSUSA/00010531/201702

Applicant: Teva B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Ganirelix - ORGALUTRAN (CAP) - PSUSA/00001517/201702

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[18] Centrally authorised products only

6.1.35. Glycopyrronium[19] - SIALANAR (CAP) - PSUSA/00010529/201703

Applicant: Proveca Limited

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Guanfacine - INTUNIV (CAP) - PSUSA/00010413/201703

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Human alfa 1-proteinase inhibitor[20] - RESPREEZA (CAP) - PSUSA/00010410/201702

Applicant: CSL Behring GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Human coagulation factor X - COAGADEX (CAP) - PSUSA/00010481/201703

Applicant: Bio Products Laboratory Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Ibritumomab tiuxetan - ZEVALIN (CAP) - PSUSA/00001704/201702

Applicant: Spectrum Pharmaceuticals B.V.

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Influenza vaccine (split virion, inactivated)[21] - IDFLU (CAP); INTANZA (CAP) - PSUSA/00001743/201703

Applicants: Sanofi Pasteur SA (IDflu), Sanofi Pasteur Europe (Intanza)

[19] Centrally authorised product indicated for the treatment of severe sialorrhea only
[20] Centrally authorised product only
[21] Centrally authorised products only

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - OPTAFLU (CAP) - PSUSA/00001745/201703

Applicant: Seqirus GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Isavuconazole - CRESEMBA (CAP) - PSUSA/00010426/201703

Applicant: Basilea Medical Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Ixekizumab - TALTZ (CAP) - PSUSA/00010493/201703

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Lapatinib - TYVERB (CAP) - PSUSA/00001829/201703

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Nalmefene - SELINCRO (CAP) - PSUSA/00010120/201702

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Naloxegol - MOVENTIG (CAP) - PSUSA/00010317/201703

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Naltrexone, bupropion - MYSIMBA (CAP) - PSUSA/00010366/201703

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Nitisinone - ORFADIN (CAP) - PSUSA/00002169/201702

Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Oritavancin - ORBACTIV (CAP) - PSUSA/00010368/201703

Applicant: The Medicines Company UK Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Ospemifene - SENSHIO (CAP) - PSUSA/00010340/201702

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Panobinostat - FARYDAK (CAP) - PSUSA/00010409/201702 (with RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Pembrolizumab - KEYTRUDA (CAP) - PSUSA/00010403/201703

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Pirfenidone - ESBRIET (CAP) - PSUSA/00002435/201702

Applicant: Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[22]) - EMEA/H/W/002300/PSUV/0022

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.55. Prasugrel - EFIENT (CAP) - PSUSA/00002499/201702

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Rasburicase - FASTURTEC (CAP) - PSUSA/00002613/201702

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.1.57. Reslizumab - CINQAERO (CAP) - PSUSA/00010523/201702

Applicant: Teva Pharmaceuticals Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. Rotigotine - LEGANTO (CAP); NEUPRO (CAP) - PSUSA/00002667/201702

Applicant: UCB Manufacturing Ireland Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.59. Ruxolitinib - JAKAVI (CAP) - PSUSA/00010015/201702

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.60. Safinamide - XADAGO (CAP) - PSUSA/00010356/201702

Applicant: Zambon S.p.A.

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.61. Sebelipase alfa - KANUMA (CAP) - PSUSA/00010422/201702

Applicant: Alexion Europe SAS

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.62. Teduglutide - REVESTIVE (CAP) - PSUSA/00009305/201702

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.63. Telavancin - VIBATIV (CAP) - PSUSA/00002879/201703

Applicant: Theravance Biopharma Ireland Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.64. Timolol, travoprost - DUOTRAV (CAP) - PSUSA/00002962/201702

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.65. Tobramycin (nebuliser solution)[23] - VANTOBRA (CAP) - PSUSA/00010370/201703

Applicant: Pari Pharma GmbH

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.66. Trastuzumab emtansine - KADCYLA (CAP) - PSUSA/00010136/201702 (with RMP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.67. Ulipristal acetate[24] - ESMYA (CAP) - PSUSA/00009325/201702

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[23] Centrally authorised product only
[24] Treatment of moderate to severe symptoms of uterine fibroids only

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

6.2.1. Imiquimod - ALDARA (CAP); ZYCLARA (CAP); NAP - PSUSA/00001729/201701

Applicants: Meda AB (Aldara, Zyclara), various

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Voriconazole - VFEND (CAP); NAP - PSUSA/00003127/201702

Applicants: Pfizer Limited (Vfend), various

PRAC Rapporteur: Menno van der Elst

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. Amisulpride (NAP) - PSUSA/00000167/201701

Applicant(s): various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Amitriptyline hydrochloride, chlordiazepoxide (NAP) - PSUSA/00000171/201702

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Amlodipine (NAP) - PSUSA/00000174/201703

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Beta-alanine (NAP) - PSUSA/00010510/201701

Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Bilastine (NAP) - PSUSA/00003163/201703

Applicant(s): various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Carbomers (NAP) - PSUSA/00000557/201701

Applicant(s): various

PRAC Lead: Gabriela Jazbec

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Cilostazol (NAP) - PSUSA/00010209/201702

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Ethinylestradiol, gestodene[25] (NAP) - PSUSA/00010145/201702

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Flubendazole (NAP) - PSUSA/00001400/201702

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

[25] Transdermal application only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Haemophilus type b and meningococcal group c conjugate vaccine (NAP) - PSUSA/00001583/201702

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Haemophilus type b conjugate vaccines (NAP) - PSUSA/00001584/201702

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Human coagulation factor VIII[26] (NAP) - PSUSA/00009174/201702

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Hydroxyethyl starch (NAP) - PSUSA/00001694/201703

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Ipratropium (NAP) - PSUSA/00001780/201701

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[26] Inhibitor bypassing fraction only

6.3.15. Ipratropium, salbutamol (NAP) - PSUSA/00001781/201701

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Levosalbutamol, salbutamol (NAP) - PSUSA/00010330/201701

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Lisdexamfetamine (NAP) - PSUSA/00010289/201702

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Loratadine (NAP) - PSUSA/00001907/201702

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Loratadine, pseudoephedrine (NAP) - PSUSA/00001908/201702

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Moxonidine (NAP) - PSUSA/00002095/201701

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Olodaterol (NAP) - PSUSA/00010245/201703

Applicant(s): various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Omega-3-acid-ethyl esters (NAP) - PSUSA/00010312/201701

Applicant(s): various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Oxatomide (NAP) - PSUSA/00002233/201701

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Saccharomyces boulardii (NAP) - PSUSA/00009284/201702

Applicant(s): various

PRAC Lead: Eva Jirsova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Tick-borne encephalitis vaccine (inactivated) (NAP) - PSUSA/00002951/201701

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Zanamivir (NAP) - PSUSA/00003141/201701

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Atazanavir, atazanavir sulfate - REYATAZ (CAP) - EMEA/H/C/000494/LEG 083.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Caroline Laborde

Scope: MAH's response to LEG 083 [comprehensive review of congenital anomalies reported with atazanavir, including a literature review and a discussion of the data gathered from the antiretroviral pregnancy registry (APR)] as per the request for supplementary information (RSI) adopted at the October 2016 PRAC meeting

Action: For adoption of advice to CHMP

6.4.2. Desloratadine - AERIUS (CAP) - EMEA/H/C/000313/LEG 066

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: Detailed review on movement disorders (including dystonia, tics and extrapyramidal symptoms) including a discussion on the need to update the product information with 'movement disorders' as applicable as requested in the conclusions of PSUSA/00000962/201607 adopted in March 2017

Action: For adoption of advice to CHMP

6.4.3. Desloratadine - AZOMYR (CAP) - EMEA/H/C/000310/LEG 066

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: Detailed review on movement disorders (including dystonia, tics and extrapyramidal symptoms) including a discussion on the need to update the product information with 'movement disorders' as applicable as requested in the conclusions of PSUSA/00000962/201607 adopted in March 2017

Action: For adoption of advice to CHMP

6.4.4. Desloratadine - NEOCLARITYN (CAP) - EMEA/H/C/000314/LEG 066

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: Detailed review on movement disorders (including dystonia, tics and extrapyramidal symptoms) including a discussion on the need to update the product information with 'movement disorders' as applicable as requested in the conclusions of

PSUSA/00000962/201607 adopted in March 2017

Action: For adoption of advice to CHMP

6.4.5. Desloratadine, pseudoephedrine sulphate - AERINAZE (CAP) - EMEA/H/C/000772/LEG 015

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: Detailed review on movement disorders (including dystonia, tics and extrapyramidal symptoms) including a discussion on the need to update the product information with 'movement disorders' as applicable as requested in the conclusions of PSUSA/00000962/201607 adopted in March 2017

Action: For adoption of advice to CHMP

6.4.6. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/LEG 156

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Detailed cumulative safety review of the safety concerns in the currently approved EU-RMP (i.e. important identified risks, important potential risks or missing information) that could be reclassified or deleted based on the available cumulative safety data, as requested in the conclusions of PSUSA/00010231/201608 adopted in April 2017

Action: For adoption of advice to CHMP

6.4.7. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/LEG 039.2

Applicant: Bayer AG

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's response to LEG 039 [cumulative review on cases of liver-related events (hepatotoxicity) as requested in the recommendation of PSUSA/00002653/201509 adopted by PRAC in April 2016] as per the request for supplementary information (RSI) adopted in March 2017

Action: For adoption of advice to CHMP

6.4.8. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/LEG 017.1

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 017 [detailed review on arterial and venous thromboembolic events (ATE/VTE) including a discussion on the biological plausibility based on the mechanism of action of ulipristal acetate, focusing on the role of oestrogen and progesterone as requested in the conclusions of PSUSA/00009325/201602 adopted by PRAC

and CHMP in September 2016] as per the request for supplementary information (RSI) adopted in February 2017

Action: For adoption of advice to CHMP

6.4.9. Vemurafenib - ZELBORAF (CAP) - EMEA/H/C/002409/LEG 035

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Review of cases of posterior reversible encephalopathy syndrome (PRES) as requested in the conclusions of PSUSA/00009329/201608 adopted in March 2017

Action: For adoption of advice to CHMP

6.4.10. Vemurafenib - ZELBORAF (CAP) - EMEA/H/C/002409/LEG 036

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Review of cases of sarcoidosis as requested in the conclusions of PSUSA/00009329/201608 adopted in March 2017

Action: For adoption of advice to CHMP

6.4.11. Vemurafenib - ZELBORAF (CAP) - EMEA/H/C/002409/LEG 037

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Cumulative review of cases of lymphopenia as requested in the conclusions of PSUSA/00009329/201608 adopted in March 2017

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

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

7.1.1. Ivabradine – CORLENTOR (CAP), IVABRADINE ANPHARM (CAP), PROCOROLAN (CAP) - EMEA/H/C/PSA/S/0022

Applicant(s): Les Laboratoires Servier (Corlentor, Procorolan), Anpharm Przedsiebiorstwo (Ivabradine Anpharm)

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for a drug utilisation study (DUS) in select European countries: a multinational, retrospective, observational study to assess effectiveness of risk-minimisation

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

measures

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

7.1.2. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSA/S/0016.1

Applicant(s): Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of an 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

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

7.1.3. Levonorgestrel (NAP) - EMEA/H/N/PSA/S/0020.1

Applicant(s): Bayer Pharma AG (Jaydess, Luadei); various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Amendment to the previously agreed protocol (version 2.2) for EURAS-LCS12 study: a European active surveillance study of LCS-12 (levonorgestrel intrauterine contraceptive system releasing 12 mcg levonorgestrel/24h in vitro), an intra-uterine device (IUD) for Jaydess and Luadei (levonorgestrel) to investigate whether LCS-12 is associated with an increased risk of unintended pregnancy compared to Mirena and to copper IUDs (previous conclusions of procedure EMEA/H/N/PSA/j/0006.1 adopted by PRAC in September 2016) as per the request for supplementary information (RSI) agreed in the conclusions of procedure EMEA/H/N/PSA/S/0020 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. Agomelatine - THYMANAX (CAP) - EMEA/H/C/000916/MEA 026.3

Applicant: Servier (Ireland) Industries Ltd.

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: MAH's response to MEA 026.2 [amendment to the protocol for cross sectional study CLE-20098-96-096: a non-interventional PASS: drug utilisation study (DUS) in selected European countries: a multinational, observational study to assess the effectiveness of risk-minimisation measures] 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. Agomelatine - VALDOXAN (CAP) - EMEA/H/C/000915/MEA 026.3

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: MAH's response to MEA 026.2 [amendment to the protocol for cross sectional study CLE-20098-96-096: a non-interventional PASS: drug utilisation study (DUS) in selected European countries: a multinational, observational study to assess the effectiveness of risk-minimisation measures] as per the request for supplementary information (RSI) adopted in June 2017

Action: For adoption of advice to CHMP

7.2.3. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/MEA 045.2

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 045.1 [PASS protocol for study GS-EU-276-4027, a drug utilisation study (DUS) to characterize: 1) prescribers' level of knowledge about the key risks of Truvada for a pre-exposure prophylaxis (PrEP) indication and assess the effectiveness of risk minimisation measures; 2) prescribing practices in routine clinical practice of Truvada for PrEP by describing the demographics of human immunodeficiency virus (HIV)-1 uninfected individuals who were prescribed Truvada for PrEP, and the prescribed dosing schedule for Truvada for PrEP as reported by the prescriber, as a result of variation II/0126 finalised at CHMP/PRAC in July 2016 to extend the indication to PrEP] as per the request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

7.2.4. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/MEA 002

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Julie Williams

Scope: Protocol for a study/survey listed in the RMP as category 3 to measure the effectiveness of Suliqua educational materials set up to evaluate the knowledge and understanding of the key safety messages in the healthcare professional guide and the patient guide

Action: For adoption of advice to CHMP

7.2.5. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 004.3

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 004.2 [revised PASS protocol for study NB-452: a cross-sectional survey to evaluate the effectiveness of the Mysimba physician prescribing checklist

(PPC) among physicians in the EU] as per request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

7.2.6. Nusinersen - SPINRAZA (CAP) - EMEA/H/C/004312/MEA 002

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Synopsis for a protocol for a prospective longitudinal neuromuscular disease (NMD) registry in a research agreement with the Muscular Dystrophy Association (MDA) U.S: descriptive characteristics of individuals with spinal muscular atrophy (SMA)

Action: For adoption of advice to CHMP

7.2.7. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.1

Applicant: AbbVie Limited

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA-002 [registry protocol for a prospective observational study P16-562 to assess the long term safety profile of venetoclax in a Swedish cohort of chronic lymphocytic leukaemia (CLL) patients] as per the request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

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

7.3.1. Hydroxyethyl starch (NAP) - EMEA/H/N/PSR/S/0009

Applicant(s): Fresenius Kabi Deutschland GmbH (Volulyte, Voluven)

PRAC Rapporteur: Qun-Ying Yue

Scope: Results of a retrospective drug utilisation study (DUS) to investigate the routine use of hydroxyethyl starch (HES)-containing infusion solutions in hospital settings

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

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

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

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. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0062

Applicant: Genzyme Europe BV

PRAC Rapporteur: Caroline Laborde

Scope: Submission of the final study report for study ALGMYC08432: a non-interventional, non-imposed PASS entitled: 'Myozyme (alglucosidase alfa) safety information packet (SIP) effectiveness evaluation: a healthcare professional (HCP) survey' (Myozyme SIP EU HCP survey). The RMP (version 8.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0045

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report for study 109MS419 (listed as a category 3 study in the RMP): a retrospective, multicentre, observational study aimed to assess the effect of Tecfidera delayed-release capsules on lymphocyte subsets in patients with relapsing forms of multiple sclerosis

Action: For adoption of PRAC Assessment Report

7.4.4. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/II/0054

Applicant: Hospira UK Limited

[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

PRAC Rapporteur: Patrick Batty

Scope: Submission of the final study report for a post-marketing surveillance study for Inflectra 100 mg (infliximab) to evaluate its safety and efficacy in Korea: study intended to identify any unexpected adverse events, serious adverse events and frequencies, pattern of occurrence of adverse events under the condition of general clinical practice as well as to determine any factor that may affect the safety and efficacy

Action: For adoption of PRAC Assessment Report

7.4.5. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/II/0045

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Patrick Batty

Scope: Submission of the final study report for a post-marketing surveillance study for Remsima 100 mg (infliximab) to evaluate its safety and efficacy in Korea: study intended to identify any unexpected adverse events, serious adverse events and frequencies, pattern of occurrence of adverse events under the condition of general clinical practice as well as to determine any factor that may affect the safety and efficacy

Action: For adoption of PRAC Assessment Report

7.4.6. Human rotavirus, live attenuated - ROTARIX (CAP) - EMEA/H/C/000639/II/0100

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report for study ROTA-085-PMS (115927) (listed as a category 3 study in the RMP): an observational prospective cohort study investigating the incidence of intussusception after vaccination for rotavirus gastroenteritis, conducted to determine the incidence of intussusception after vaccination with Rotarix in Japan. The RMP (version 19) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

Applicant: Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

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

Action: For adoption of PRAC Assessment Report

7.4.8. 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

7.4.9. Trastuzumab - HERCEPTIN (CAP) - EMEA/H/C/000278/II/0135

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report for study BO20652 (OHERA): a non-interventional study aimed to determine the incidence of symptomatic congestive heart failure and cardiac death in patients with human epidermal growth factor 2 (HER2)-positive early breast cancer treated with Herceptin (trastuzumab) as per routine clinical practice. This study is listed as a category 3 study in the RMP. The RMP (version 18.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/MEA 005.4

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reports from rheumatoid arthritis registries from the US National Databank of Rheumatic Diseases (RA0005), German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) (RA0020), Register for Antirheumatic Therapies in Sweden (ARTIS) (RA0021), British Society for Rheumatology Biologicals Register (BSRBR) (RA0022)

Action: For adoption of advice to CHMP

7.5.2. Efavirenz, emtricitabine, tenofovir disoproxil - ATRIPLA (CAP) - EMEA/H/C/000797/MEA 039.6

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd.

PRAC Rapporteur: Martin Huber

Scope: Fourth annual report for malignant events associated with efavirenz: Diagnostic Consulting Network (DCN) report as a routine risk minimisation measures

Action: For adoption of advice to CHMP

7.5.3. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 006.2

Applicant: Hexal AG

PRAC Rapporteur: Patrick Batty

Scope: Sixth annual interim safety report for study EP006-401: safety follow-up of severe chronic neutropenia (SCN) patients included in phase IV study: safety data collected via cooperation with the Severe Chronic Neutropenia International Registry and reported annually. Patients are followed-up for a total of five years (one year in the SCN study and four years within the registry) [final clinical study report (CSR) due date: 31/12/2019]

Action: For adoption of advice to CHMP

7.5.4. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 007.3

Applicant: Hexal AG

PRAC Rapporteur: Patrick Batty

Scope: Sixth annual interim result for study EP06-501: a non-interventional, prospective, long-term safety data collection for Filgrastim Hexal and Zarzio in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell mobilisation (SMART) [final clinical study report (CSR) due date: 31/12/2019]

Action: For adoption of advice to CHMP

7.5.5. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 006.2

Applicant: Sandoz GmbH

PRAC Rapporteur: Patrick Batty

Scope: Sixth annual interim safety report for study EP006-401: safety follow-up of severe chronic neutropenia (SCN) patients included in phase IV study: safety data collected via cooperation with the Severe Chronic Neutropenia International Registry and reported annually. Patients are followed-up for a total of five years (one year in the SCN study and four years within the registry) [final clinical study report (CSR) due date: 31/12/2019]

Action: For adoption of advice to CHMP

7.5.6. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.3

Applicant: Sandoz GmbH

PRAC Rapporteur: Patrick Batty

Scope: Sixth annual interim result for study EP06-501: a non-interventional, prospective, long-term safety data collection for Filgrastim Hexal and Zarzio in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell mobilisation (SMART) [final clinical study report (CSR) due date: 31/12/2019]

Action: For adoption of advice to CHMP

7.5.7. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 012.6

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: Sixth annual interim pooled report for studies D2404 (multinational Gilenya pregnancy exposure registry in multiple sclerosis (MS)), D2403 (a long-term, prospective, multinational, parallel-cohort study monitoring safety in patients with MS newly started on fingolimod once daily or treated with another approved disease-modifying therapy), D2406 (a long-term, prospective, non-interventional, multinational, parallel-cohort study monitoring safety in patients with MS newly initiated on fingolimod once daily or treated with another approved disease-modifying therapy) with the first yearly report for study D2409: a long-term, open-label, multicentre study assessing long-term cardiovascular risks in patients treated with fingolimod). This procedure also includes an annual report for the pregnancy intensive monitoring (PRIM) study

Action: For adoption of advice to CHMP

7.5.8. Florbetaben (^{18}F) - NEURACEQ (CAP) - EMEA/H/C/002553/MEA 005

Applicant: Piramal Imaging Limited

PRAC Rapporteur: Patrick Batty

Scope: Interim results for PASS study FBB-01_02_13: a prospective observational study to assess the effectiveness of the training and risk minimisation measures recommended for the usage of the diagnostic agent Neuraceq in post-authorisation clinical settings [final clinical study report (CSR): Q1/2019]

Action: For adoption of advice to CHMP

7.5.9. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 026.3

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 026.2 [first progress report for study MRK-2859: ulcerative colitis (UC) Nordic registry: a non-interventional observational longitudinal PASS of Simponi in the treatment of UC using Nordic national health registries] as per the request for supplementary information (RSI) adopted in October 2016

Action: For adoption of advice to CHMP

7.5.10. Indacaterol, glycopyrronium - ULTIBRO BREEZHALER (CAP) - EMEA/H/C/002679/ANX 002.4; ULUNAR BREEZHALER (CAP) - EMEA/H/C/003875/ANX 003.3; XOTERNA BREEZHALER (CAP) - EMEA/H/C/003755/ANX 002.4

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Third interim report for study CQVA149A2402: a multinational database cohort study to assess RMP specified safety outcomes in association with indacaterol/glycopyrronium bromide in Europe [EU PAS register ENCePP/SDPP/7674]

Action: For adoption of advice to CHMP

7.5.11. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/MEA 036.3

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to MEA 036.2 [Annual interim report (covering the period 1 February 2016 to 31 January 2017) on the effectiveness of risk minimisation measures for multiple patch use with copies of Council for International Organizations of Medical Sciences (CIOMS) reports of medication errors and misuse] as per the request for supplementary information (RSI) adopted in June 2017

Action: For adoption of advice to CHMP

7.5.12. Rivastigmine - PROMETAX (CAP) - EMEA/H/C/000255/MEA 037.3

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to MEA 037.2 [Annual interim report (covering the period 1 February 2016 to 31 January 2017) on the effectiveness of risk minimisation measures for multiple patch use with copies of Council for International Organizations of Medical Sciences (CIOMS) reports of medication errors and misuse] as per the request for supplementary information (RSI) adopted in June 2017

Action: For adoption of advice to CHMP

7.5.13. Valproate (NAP) - EMEA/H/N/PSI/J/0002

Applicant(s): Sanofi-aventis Recherche & Development (on behalf of a consortium)

PRAC Rapporteur: Sabine Straus

Scope: Second interim results report for a joint drug utilisation study (DUS) of valproate and related substances conducted in Europe aiming at describing the prescribing practices before and after the dissemination of risk minimisation measures (RMM) (i.e. educational materials and direct healthcare professional communication (DHPC)) and assessing the effectiveness of these measures using databases, as requested in the outcome of the referral procedure on valproate and related substances (EMEA/H/A-31/1387) concluded in 2014

Action: For adoption of conclusions (or request for supplementary information (RSI))

7.6. Others

7.6.1. Dexamethasone - OZURDEX (CAP) - EMEA/H/C/001140/MEA 020

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Julie Williams

Scope: Survey to evaluate the physician education component of the simplified Ozurdex (dexamethasone) educational materials in order to assess the effectiveness of the educational material provided to physicians treating patients with Ozurdex by evaluating the physicians' knowledge and understanding of the key information in the Ozurdex injector's guide

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

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

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)

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

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

8.1. Annual reassessments of the marketing authorisation

None

8.2. Conditional renewals of the marketing authorisation

8.2.1. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/R/0007 (without RMP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Patrick Batty

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - EMEA/H/C/002450/R/0015 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A., ATMP[31]

PRAC Rapporteur: Julie Williams

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0002 (without RMP), Orphan

Applicant: Intercept Pharma Ltd

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and haemophilus influenzae type B conjugate vaccine (adsorbed) - HEXYON (CAP) - EMEA/H/C/002796/R/0072 (with RMP)

Applicant: Sanofi Pasteur Europe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and haemophilus influenzae type B conjugate vaccine (adsorbed) - HEXACIMA (CAP) - EMEA/H/C/002702/R/0068 (with RMP)

Applicant: Sanofi Pasteur SA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Human normal immunoglobulin - PRIVIGEN (CAP) - EMEA/H/C/000831/R/0122 (without RMP)

Applicant: CSL Behring GmbH

[31] Advanced therapy medicinal product

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Imatinib - IMATINIB ACTAVIS (CAP) - EMEA/H/C/002594/R/0015 (without RMP)

Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Memantine - MARIXINO (CAP) - EMEA/H/C/002658/R/0012 (without RMP)

Applicant: Consilient Health Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. 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

8.3.7. Ocriplasmin - JETREA (CAP) - EMEA/H/C/002381/R/0033 (without RMP)

Applicant: ThromboGenics NV

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Pertuzumab - PERJETA (CAP) - EMEA/H/C/002547/R/0031 (without RMP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)- PREPANDRIX (CAP) - EMEA/H/C/000822/R/0071 (without RMP)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Telmisartan, hydrochlorothiazide - ACTELSAR HCT (CAP) - EMEA/H/C/002676/R/0015 (without RMP)

Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Carmela Macchiarulo

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Telmisartan, hydrochlorothiazide - TOLUCOMBI (CAP) - EMEA/H/C/002549/R/0020 (without RMP)

Applicant: Krka, d.d., Novo mesto

PRAC Rapporteur: Carmela Macchiarulo

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. 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

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

Disclosure of information on results of pharmacovigilance inspections could undermine the protection of the purpose of these inspections, investigations and audits. Therefore such

information is not reported in the agenda.

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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.

Other safety issues for discussion requested by the Member States

10.5. Safety related variations of the marketing authorisation

None

10.6. Other requests

None

11. Organisational, regulatory and methodological matters

11.1. Mandate and organisation of the PRAC

11.1.1. PRAC Brexit ancillary working group

PRAC lead: Almath Spooner

Action: For discussion

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

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

Action: For discussion

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

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

Action: For discussion

11.2. Coordination with EMA Scientific Committees or CMDh

11.2.1. Guideline on safety and efficacy follow-up – risk management plan of advanced therapy medicinal products (ATMP) – update

PRAC lead: Brigitte Keller-Stanislawski, Dolores Montero Corominas, Sabine Straus, Ulla Wändel Liminga, Julie Williams

Action: For discussion

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

None

11.4. Cooperation within the EU regulatory network

11.4.1. PRAC strategic review and learning meeting, Estonia, 16-18 October 2017

PRAC lead: Maia Uusküla

Action: For discussion

11.4.2. Reflection paper on the use of extrapolation in the development of medicines for paediatrics

Action: For adoption

11.5. Cooperation with International Regulators

None

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

None

11.7. PRAC work plan

11.7.1. PRAC work plan 2018 – preparation

PRAC lead: June Raine

Action: For discussion

11.8. Planning and reporting

11.8.1. EU Pharmacovigilance system

None

11.8.2. Marketing authorisation applications (MAA) expected for 2017 – Q3 2017 update

Action: For discussion

11.9. Pharmacovigilance audits and inspections

11.9.1. Pharmacovigilance systems and their quality systems

None

11.9.2. Pharmacovigilance inspections – template for sharing assessor's information

Action: For discussion

11.9.3. Pharmacovigilance audits - Pharmacovigilance Audit Facilitation Group (PAFG)

PRAC lead: Caitriona Fisher (PAFG chair)

Action: For discussion

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

11.10.1. Periodic safety update reports

None

11.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

11.10.3. PSURs repository

None

11.10.4. Roadmap for periodic safety update reports (PSUR) activities update: report from joint assessor-industry training, 22 September 2017

PRAC lead: Menno van der Elst, Ulla Wändel Liminga

Action: For discussion

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

Action: For adoption

11.11. Signal management

11.11.1. Good pharmacovigilance practice (GVP) module IX on Signal management – revision 1 and addendum

PRAC lead: Sabine Straus

Action: For adoption

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

PRAC lead: Sabine Straus

Action: For discussion

11.12. Adverse drug reactions reporting and additional reporting

11.12.1. Management and reporting of adverse reactions to medicinal products

None

11.12.2. Additional monitoring

None

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

Action: For adoption

11.13. EudraVigilance database

11.13.1. Activities related to the confirmation of full functionality

None

11.14. Risk management plans and effectiveness of risk minimisations

11.14.1. Risk management systems

None

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

None

11.14.3. Good pharmacovigilance practice (GVP) module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' – revision 3

PRAC lead: Sabine Straus, Torbjörn Callréus

Action: For discussion

11.15. Post-authorisation safety studies (PASS)

11.15.1. Good pharmacovigilance practices (GVP) module VIII on 'Post-authorisation safety studies (PASS)' – revision 3 in line with update of GVP module VI on 'Management and reporting of adverse reactions to medicinal products'

Action: For adoption

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

None

11.16. Community procedures

11.16.1. Referral procedures for safety reasons

None

11.17. Renewals, conditional renewals, annual reassessments

None

11.18. Risk communication and transparency

11.18.1. Good pharmacovigilance practice (GVP) module XV on 'Safety communication' – revision 1

PRAC lead: Amelia Cupelli, Sabine Straus

Action: For adoption

11.18.2. Public participation in pharmacovigilance

None

11.18.3. Safety communication

None

11.19. Continuous pharmacovigilance

11.19.1. Incident management

None

11.20. Others

11.20.1. Guideline on good pharmacovigilance practices (GVP) Annex I on 'Definitions' - revision 4

Action: For adoption

12. Any other business

13. 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/