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Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 02-05 September 2019

Chair: Sabine Straus – Vice-Chair: Martin Huber

02 September 2019, 13:00 – 19:30, room 1/C

03 September 2019, 08:30 – 19:30, room 1/C

04 September 2019, 08:30 – 19:30, room 1/C

05 September 2019, 08:30 – 16:00, room 1/C

Organisational, regulatory and methodological matters (ORGAM)

19 September 2019, 09:00-12:00, room 6/D, via teleconference

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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



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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 02-05 September 2019. See September 2019 PRAC minutes (to be published post October 2019 PRAC meeting).

1.2. Agenda of the meeting on 02-05 September 2019

Action: For adoption

1.3. Minutes of the previous meeting on 08-11 July 2019

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. Estradiol¹ (NAP) - EMEA/H/A-31/1482

Applicant(s): various

PRAC Rapporteur: Eva Jirsova; PRAC Co-rapporteur: Menno van der Elst

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

Action: For adoption of a list of experts for the ad-hoc expert group meeting

3.2.2. Tofacitinib - XELJANZ (CAP) - EMEA/H/A-20/1485

Applicant(s): Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan; PRAC Co-rapporteur: Amelia Cupelli

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

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

3.3. Procedures for finalisation

None

3.4. Re-examination procedures²

None

3.5. Others

None

¹ 0.01%, topical use only

² Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

4. Signals assessment and prioritisation³

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Adalimumab – AMGEVITA (CAP); HALIMATOZ (CAP); HEFIYA (CAP); HULIO (CAP); HUMIRA (CAP); HYRIMOZ (CAP); IMRALDI (CAP)

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Humira), Amgen Europe B.V. (Amgevita), Mylan S.A.S (Hulio), Samsung Bioepis NL B.V. (Imraldi), Sandoz GmbH (Halimatoz, Hefiya, Hyrimoz)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of pericarditis

Action: For adoption of PRAC recommendation

EPITT 19457 – New signal

Lead Member State(s): SE

4.1.2. Anastrozole (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of hallucinations

Action: For adoption of PRAC recommendation

EPITT 19449 – New signal

Lead Member State(s): LV

4.1.3. Durvalumab – IMFINZI (CAP)

Applicant(s): AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Signal of myasthenia gravis

Action: For adoption of PRAC recommendation

EPITT 19451 – New signal

Lead Member State(s): NO

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

4.1.4. Ibrutinib – IMBRUVICA (CAP)

Applicant(s): Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Signal of neutrophilic dermatoses

Action: For adoption of PRAC recommendation

EPITT 19444 – New signal

Lead Member State(s): HR

4.1.5. Immune checkpoint inhibitors: atezolizumab – TECENTRIQ (CAP); avelumab – BAVENCIO (CAP); cemiplimab – LIBTAYO (CAP); durvalumab – IMFINZI (CAP); ipilimumab – YERVOY (CAP); nivolumab – OPDIVO (CAP); pembrolizumab – KEYTRUDA (CAP)

Applicant(s): AstraZeneca AB (Imfinzi), Bristol-Myers Squibb Pharma (Opdivo), Bristol-Myers Squibb Pharma EEIG (Yervoy), Merck Europe B.V. (Bavencio), Merck Sharp & Dohme B.V. (Keytruda), Regeneron Ireland U.C. (Libtayo), Roche Registration GmbH (Tecentriq)

PRAC Rapporteur: To be appointed

Scope: Signal of tuberculosis

Action: For adoption of PRAC recommendation

EPITT 19464 – New signal

Lead Member State(s): DK, NL, NO, PT

4.1.6. Prasugrel – EFIENT (CAP), PRASUGREL MYLAN (CAP), NAP

Applicant(s): Daiichi Sankyo Europe GmbH (Efient), Mylan S.A.S (Prasugrel Mylan), various

PRAC Rapporteur: To be appointed

Scope: Signal of severe cutaneous adverse reactions (SCARs)

Action: For adoption of PRAC recommendation

EPITT 19463 – New signal

Lead Member State(s): DK

4.1.7. Sacubitril, valsartan – ENTRESTO (CAP); NEPARVIS (CAP)

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Anette Kristine Stark

Scope: Signal of ventricular arrhythmia

Action: For adoption of PRAC recommendation

EPITT 19448 – New signal

Lead Member State(s): DK

4.2. New signals detected from other sources

- 4.2.1. Abiraterone – ZYTIGA (CAP);
Sulphonylureas: glibenclamide – AMGLIDIA (CAP), NAP; gliclazide (NAP); gliquidone (NAP); glimepiride (NAP); glimepiride, pioglitazone – TANDEMACT (CAP); glipizide (NAP); tolbutamide (NAP);
-

Applicant(s): Ammtek (Amglidia), Janssen-Cilag International NV (Zytiga), Takeda Pharma A/S (Tandemact), various

PRAC Rapporteur: To be appointed

Scope: Signal of interaction with sulphonylureas leading to hypoglycaemia

Action: For adoption of PRAC recommendation

EPITT 19445 – New signal

Lead Member State(s): BE, DK, ES, FR, HR, IE, IS, NL

- 4.2.2. Golimumab – SIMPONI (CAP)
-

Applicant(s): Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of inflammatory myopathy

Action: For adoption of PRAC recommendation

EPITT 19460 – New signal

Lead Member State(s): SE

- 4.2.3. Sitagliptin – JANUVIA (CAP), RISTABEN (CAP), TESAVEL (CAP), XELEVIA (CAP);
NAP
sitagliptin, ertugliflozin – STEGLUJAN (CAP)
sitagliptin, metformin – EFFICIB (CAP); JANUMET (CAP); VELMETIA (CAP); NAP
-

Applicant(s): Merck Sharp & Dohme B.V., various

PRAC Rapporteur: Menno van der Elst

Scope: Signal of rhabdomyolysis

Action: For adoption of PRAC recommendation

EPITT 19466 – New signal

Lead Member State(s): NL

4.3. Signals follow-up and prioritisation

- 4.3.1. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/SDA/029
-

Applicant(s): Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Signal of ischemic stroke

Action: For adoption of PRAC recommendation

EPITT 19369 – Follow-up to April 2019

4.3.2. [Ibuprofen \(NAP\) and fixed-dose combinations: chlorphenamine, ibuprofen, phenylephrine \(NAP\); dimenhydrinate, ibuprofen, caffeine \(NAP\); ibuprofen, ascorbic acid \(NAP\); ibuprofen, caffeine \(NAP\); ibuprofen, codeine \(NAP\); ibuprofen, hydrocodone \(NAP\); ibuprofen, paracetamol \(NAP\); ibuprofen, phenylephrine \(NAP\); ibuprofen, pseudoephedrine \(NAP\)](#)

Applicant(s): various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of acute generalised exanthematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 19409 – Follow-up to May 2019

4.3.3. [Omalizumab - XOLAIR \(CAP\) - EMEA/H/C/000606/SDA/068](#)

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Signal of acquired haemophilia

Action: For adoption of PRAC recommendation

EPITT 19385 – Follow-up to April 2019

4.3.4. [Pembrolizumab - KEYTRUDA \(CAP\) - EMEA/H/C/003820/SDA/022](#)

Applicant(s): Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Signal of optic neuritis

Action: For adoption of PRAC recommendation

EPITT 19381 – Follow-up to April 2019

4.3.5. [Perampanel - FYCOMPA \(CAP\) - EMEA/H/C/002434/SDA/018](#)

Applicant(s): Eisai GmbH

PRAC Rapporteur: Ghania Chamouni

Scope: Signal of hepatotoxicity

Action: For adoption of PRAC recommendation

EPITT 19383 – Follow-up to April 2019

4.3.6. Sodium-glucose co-transporter 2 (SGLT2) inhibitors:
canagliflozin – INVOKANA (CAP) - EMEA/H/C/002649/SDA/018; canagliflozin,
metformin – VOKANAMET (CAP) - EMEA/H/C/002656/SDA/016; dapagliflozin –
EDISTRIDE (CAP) - EMEA/H/C/004161/SDA/014; dapagliflozin – FORXIGA (CAP) -
EMEA/H/C/002322/SDA/027; dapagliflozin, metformin – EBYMECT (CAP) -
EMEA/H/C/004162/SDA/013; dapagliflozin, metformin – XIGDUO (CAP) -
EMEA/H/C/002672/SDA/016; empagliflozin – JARDIANCE (CAP) -
EMEA/H/C/002677/SDA/017; empagliflozin, metformin – SYNJARDY (CAP) -
EMEA/H/C/003770/SDA/011; empagliflozin, linagliptin – GLYXAMBI (CAP) -
EMEA/H/C/003833/SDA/008; ertugliflozin – STEGLATRO (CAP) -
EMEA/H/C/004315/SDA/006; ertugliflozin, metformin – SEGLUROMET (CAP) -
EMEA/H/C/004314/SDA/005; ertugliflozin, sitagliptin - STEGLUJAN (CAP) -
EMEA/H/C/004313/SDA/006; saxagliptin, dapagliflozin - QTERN (CAP) -
EMEA/H/C/004057/SDA/002

Applicant(s): AstraZeneca AB (Ebymect, Edistride, Forxiga, Qtern, Xigduo), Boehringer
Ingelheim (Glyxambi), Boehringer Ingelheim International GmbH (Jardiance, Synjardy),
Janssen-Cilag International NV (Invokana, Vokanamet), Merck Sharp & Dohme B.V.
(Segluromet, Steglatro, Steglujan)

PRAC Rapporteur: Martin Huber

Scope: New information on the known association between sodium-glucose co-transporter 2
(SGLT2) inhibitors and diabetic ketoacidosis (DKA) in surgical patients

EPITT 19355 – Follow-up to March 2019

4.3.7. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/SDA/007

Applicant(s): Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Signal of psoriasis

Action: For adoption of PRAC recommendation

EPITT 19366 – Follow-up to April 2019

4.3.8. Ticagrelor - BRILIQUE (CAP) - EMEA/H/C/001241/SDA/025

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Signal of severe cutaneous adverse reactions (SCARs)

Action: For adoption of PRAC recommendation

EPITT 19375 – Follow-up to April 2019

4.3.9. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/SDA/058

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)

Action: For adoption of PRAC recommendation

EPITT 19360 – Follow-up to March 2019

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Alpelisib - EMEA/H/C/004804

Scope: Treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, advanced breast cancer with a phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alfa (PIK3CA) mutation in combination with fulvestrant after disease progression following an endocrine-based regimen

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

5.1.2. Deferasirox - EMEA/H/C/005156

Scope: Treatment of chronic iron overload

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

5.1.3. Dexmedetomidine - EMEA/H/C/005152

Scope: Sedation of adult intensive care unit (ICU) patients requiring a sedation level not deeper than arousal in response to verbal stimulation, and sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation

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

5.1.4. Selinexor - EMEA/H/C/005127, Orphan

Applicant: Karyopharm Europe GmbH

Scope (accelerated assessment): Treatment of patients with relapsed refractory multiple myeloma (RRMM)

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

5.1.5. Sodium oxybate - EMEA/H/C/004962

Scope: Medium to long-term maintenance of alcohol abstinence and treatment of mild to moderate alcohol withdrawal syndrome

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

5.1.6. Upadacitinib - EMEA/H/C/004760

Scope: Treatment of moderate to severe active rheumatoid arthritis

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. Aliskiren - RASILEZ (CAP) - EMEA/H/C/000780/WS1581/0123; Aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/WS1581/0093

Applicant: Noden Pharma DAC

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of an updated RMP (version 14) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and in line with revision 2 of the guidance on the format of RMP in the EU (template). The update also includes the addition of the new important potential risk of non-melanoma skin cancer (related to Rasilez HCT (aliskiren/hydrochlorothiazide) only) as per the final recommendation of the signal on hydrochlorothiazide-containing products and skin cancer (EPITT 19138) adopted in September 2018

Action: For adoption of PRAC Assessment Report

5.2.2. Brinzolamide, brimonidine - SIMBRINZA (CAP) - EMEA/H/C/003698/II/0019

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP (version 3.0) in order to remove 'metabolic acidosis/renal impairment' as an important potential risk from the list of safety concerns and to bring it in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.3. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0013

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 4.0-s1) to remove 'exposure during lactation' as missing information based on a literature review

Action: For adoption of PRAC Assessment Report

5.2.4. Human normal immunoglobulin - KIOVIG (CAP) - EMEA/H/C/000628/II/0091

Applicant: Baxter AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 9.0) in order to include 'chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)' as a new indication and update the list of safety concerns to bring it in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.5. [Lutropin alfa - LUVERIS \(CAP\) - EMEA/H/C/000292/II/0082](#)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 3.1) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and to remove 'ovarian hyperstimulation syndrome (OHSS)' and 'mild to severe hypersensitivity reactions including anaphylactic reactions and shock' as important identified risks and well as 'thromboembolic (TE) events', 'reproductive system cancer', 'ectopic pregnancy', 'multiple pregnancies', 'congenital anomaly' and 'off label use' as important potential risks. In addition, the age for missing information 'hypogonadotropic hypogonadal women with severe luteinizing hormone (LH) and follicle-stimulating hormone (FSH) deficiency of advanced maternal age (older than 40 years)' is changed from 40 to 42 years. Finally, the sections on epidemiology and non-clinical sections are updated as per the most recent data

Action: For adoption of PRAC Assessment Report

5.2.6. [Melatonin - SLENYTO \(CAP\) - EMEA/H/C/004425/II/0010](#)

Applicant: RAD Neurim Pharmaceuticals EEC SARL

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 1.3) to remove 'delay of sexual maturation and development' as an important potential risk based on the results of study NEUCH7911 showing a lack of effect on sexual maturation and growth after 2 years of continuous treatment, and temporary recommendation for use (RTU) data demonstrating a lack of effect on growth after continuous use of up to 3 years

Action: For adoption of PRAC Assessment Report

5.2.7. [Pazopanib - VOTRIENT \(CAP\) - EMEA/H/C/001141/II/0054](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 17.0) in order to postpone the submission due date for the clinical study report (CSR) for study VEG108844 (COMPARZ): a study of pazopanib versus sunitinib in the treatment of subjects with locally advanced and/or metastatic renal cell carcinoma, and its sub-studies. In addition, the RMP is updated to reflect PRAC recommendations for additional assessments of some risks and to revise the categorisation of the safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.8. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/II/0051, Orphan

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Annika Folin

Scope: Submission of an updated RMP (version 19) in order to reflect deletion/changes in the categorisation of safety concerns in line with revision 2 of GVP module V on 'Risk management systems'. In addition, the RMP is updated to reflect the change of categorisation of posterior reversible encephalopathy syndrome (PRES) as requested in the conclusions of PSUSA/00010128/201712 procedure adopted in July 2018; to correct the categorisation of study AP24534-14-203: a randomised, open-label, phase 2 trial of ponatinib in patients with resistant chronic phase chronic myeloid leukaemia to characterize the efficacy and safety of a range of doses, from a category 3 study to category 1 study in the RMP and Annex II and to revise the due date for the submission of its study report to August 2021, as described in the product information and as agreed in the conclusions of ANX 016 procedure adopted by CHMP in September 2017

Action: For adoption of PRAC Assessment Report

5.2.9. Safinamide - XADAGO (CAP) - EMEA/H/C/002396/II/0031

Applicant: Zambon S.p.A.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP (version 6.0) in order to implement changes in line with revision 2 of the guidance on the format of RMP in the EU (template) and to introduce changes to pre-clinical, clinical and post-marketing exposure information, and to update the due date of drug utilisation study (DUS) Z7219N02: a European multicentre retrospective-prospective cohort study to observe safinamide safety profile and pattern of use in clinical practice during the first post-commercialisation phase; from July 2019 to 28 February 2020

Action: For adoption of PRAC Assessment Report

5.2.10. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II//0034

Applicant: Amgen Europe B.V., ATMP⁴

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 7.0) in order to add two studies listed as category 3 studies in the RMP, namely: study 20180062: a multinational, non-interventional, cross-sectional survey in patients ≥ 18 years of age who have received talimogene laherparepvec at least once in the 3 months before completion of the survey to evaluate the effectiveness of the patient-directed additional risk minimisation measures (RMMs); and study 20180099: a multinational, non-interventional, cross-sectional survey in physicians who completed the required talimogene laherparepvec training as part of the controlled distribution program to evaluate the effectiveness of the HCP-directed additional RMMs. In addition, the RMP is updated to include an internal evaluation of managed

⁴ Advanced Therapy Medicinal Product

distribution process metrics, to evaluate the effectiveness of additional risk minimisation measures (aRMM)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/II/0002

Applicant: Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study report for study ANNEXA-4 (listed as category 2 study in Annex II and the RMP): an interventional non-randomized, multicentre, prospective, open-label, single-group study in andexanet alfa patients receiving a factor Xa inhibitor with acute major bleeding. The RMP (version 1.1) is updated accordingly

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

5.3.2. Anidulafungin - ECALTA (CAP) - EMEA/H/C/000788/II/0040

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of the approved indication 'treatment of invasive candidiasis (ICC)' to include paediatric patients aged from 1 month to less than 18 years of age. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated accordingly. The RMP is also updated in line with revision 2 of GVP module V on 'Risk management systems'. In addition, the MAH took the opportunity to update the information in the product information on fructose in line with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.3. Apalutamide - ERLEADA (CAP) - EMEA/H/C/004452/II/0001

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Extension of indication to include the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT) for Erleada (apalutamide) based on the results of study 56021927PCR3002 (TITAN study): a randomised, double-blind, placebo-controlled phase 3 study comparing apalutamide plus ADT versus ADT in patients with mHSPC. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add a warning on ischaemic cardiovascular events and to reflect new safety and efficacy information. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to introduce editorial updates to the product information

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

5.3.4. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/II/0009/G, Orphan

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Grouped variations consisting of: 1) extension of indication to include a new indication as the first-line combination treatment with avelumab and axitinib in adult patients with advanced renal cell carcinoma (aRCC). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 1.7) are updated accordingly; 2) change in section 4.2 of the SmPC to support the switch of avelumab dosing regimen from 10 mg/kg every two weeks (weight-based) to a flat dose of 800 mg every two weeks applicable to the new proposed indication aRCC and the existing one on Merkel cell carcinoma (MCC). The MAH took the opportunity to introduce some editorial changes in the product information

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

5.3.5. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/II/0033/G, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) extension of indication to include patients 12 years of age and older based on week 24 analysis of cohort 1 (adolescent subjects aged ≥ 12 to < 18 years) for study TMC207-TIDP59-C211: a phase 2, open-label, multicentre, single-arm study to evaluate the pharmacokinetics, safety, tolerability and anti-mycobacterial activity of bedaquiline (TMC207) in combination with a background regimen (BR) of multidrug resistant tuberculosis (MDR-TB) medications for the treatment of children and adolescents 0 month to < 18 years of age who have confirmed a probable pulmonary MDR-TB. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.2) are updated accordingly; 2) update of section 4.9 of the SmPC to remove reference to the use of activated charcoal as an aid to remove unabsorbed bedaquiline in case of overdose

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

5.3.6. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0062

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include patients aged 5 years and older in the current approved indication for the powder for solution for infusion 120 mg/mL and 400 mg/mL based on the results of study BEL114055: a multicentre, randomised parallel group, placebo-controlled double-blind trial to evaluate the safety, efficacy, and pharmacokinetics of belimumab, a human monoclonal anti-BLyS antibody, plus standard therapy in paediatric patients with systemic lupus erythematosus (SLE). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated with safety and efficacy information. In

addition, sections 4.2, 5.1 and 5.2 of the SmPC for the solution for injection in pre-filled pen and pre-filled syringe 200 mg are updated to reflect the paediatric data available for the intravenous formulation. The package leaflet is updated accordingly. Furthermore, the RMP (version 28.0) is updated accordingly and with revision 2 of the guidance on the format of RMP in the EU (template). Finally, the MAH took the opportunity to introduce some editorial changes in the product information and bring it in line with the latest quality review document (QRD) template (version 10.0)

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

5.3.7. Bevacizumab - AVASTIN (CAP) - EMEA/H/C/000582/II/0110

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of the final report from study NEJ026 (listed as a category 1/obligation in Annex II): an open-label, randomized, phase 3 study conducted in Japan to compare erlotinib + bevacizumab combination therapy versus erlotinib monotherapy as first-line therapies for patients with non-small-cell lung carcinoma (NSCLC) with epidermal growth factor receptor (EGFR) gene mutations (exon 19 deletion or exon 21 L858R substitution). The RMP (version 30.0) is updated accordingly. In addition, the package leaflet is updated to reflect information on sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.8. Bosentan - STAYVEER (CAP) - EMEA/H/C/002644/II/0028

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Adrien Inoubli

Scope: Update of Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' in order to remove the 'prescriber kit' from the additional risk minimisation measures (aRMM) and also to remove the obligation to implement a formal 'controlled distribution system' in EU countries as requested in the conclusions of LEG 10.2 adopted by PRAC in March 2019. Section 4.2 of the SmPC is updated to include the statement that patients should be given the Package leaflet and the patient alert card which are included in the pack. The RMP (version 11) is updated accordingly. In addition, the MAH took the opportunity to align the product information with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.9. Bosentan - TRACLEER (CAP) - EMEA/H/C/000401/II/0092

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Adrien Inoubli

Scope: Update of Annex II-D on 'Conditions or restrictions with regard to the safe and

effective use of the medicinal product' in order to remove the 'prescriber kit' from the additional risk minimisation measures (aRMM) and also to remove the obligation to implement a formal 'controlled distribution system' in EU countries as requested in the conclusions of LEG 86.2 adopted by PRAC in March 2019. Section 4.2 of the SmPC is updated to include the statement that patients should be given the Package leaflet and the patient alert card which are included in the pack. The RMP (version 11) is updated accordingly. In addition, the MAH took the opportunity to align the product information with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.10. Brigatinib - ALUNBRIG (CAP) - EMEA/H/C/004248/II/0003

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously untreated with an ALK inhibitor for Alunbrig (brigatinib). The addition of a new indication is supported by data from study AP26113-13-301 (ALTA 1L): a phase 3, randomized, open label, comparative, multicentre, international phase 3 study of brigatinib versus crizotinib in patients With ALK-positive advanced lung cancer. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet, labelling and the RMP (version (version 5.1) are updated accordingly. The MAH took the opportunity to introduce minor editorial corrections in the product information

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/0043, Orphan

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a systematic literature analysis to fulfil a specific obligation (SOB) to provide comparative data on efficacy, including pooled outcomes of patients with veno-occlusive disease (VOD) treated with defibrotide; VOD incidence and outcomes in patients not treated with defibrotide. As a consequence, Annex II and the RMP (version 6.1) are updated. In addition, the due date of the observational DefiFrance study (listed as a category 3 study in the RMP): a national, post-registration, observational study of the long term safety and health outcome of patients treated with Defitelio (defibrotide) including patients with severe hepatic VOD after haematopoietic stem cell transplantation (HSCT), is revised. Finally, the RMP is updated in line with revision 2 of the guidance on the format of RMP in the EU (template). The MAH took the opportunity to introduce minor editorial corrections

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

5.3.12. Docetaxel - DOCETAXEL ZENTIVA (CAP) - EMEA/H/C/000808/WS1550/0058; Docetaxel - TAXOTERE (CAP) - EMEA/H/C/000073/WS1550/0131

Applicant: Aventis Pharma S.A.

PRAC Rapporteur: Ghania Chamouni

Scope: Extension of indication to include combination with androgen-deprivation therapy (ADT), with or without prednisone or prednisolone, for the treatment of patients with metastatic hormone-sensitive prostate cancer for Taxotere (docetaxel) and Docetaxel Zentiva (docetaxel). As a consequence, sections 4.1, 4.2, 4.4 and 4.8 of the SmPC are updated. The package leaflet and the RMP (version 1.0) are updated accordingly. In addition, the MAH took the opportunity to update information impacting the local representatives in the package leaflet

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

5.3.13. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0040

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Extension of indication to include a new indication to reduce the risk of major adverse cardiovascular events (MACE) (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus (T2DM) who have multiple cardiovascular risk factors without established cardiovascular disease, and in adults with T2DM with established cardiovascular disease. The data supporting this new indication is derived from study GBDJ (researching cardiovascular events with a weekly incretin in diabetes (REWIND)): a single pivotal phase 3 long-term cardiovascular outcomes study, which assessed the efficacy and safety of treatment with once-weekly injection of dulaglutide 1.5 mg when added to glucose-lowering regimen of patients with T2DM, compared to the addition of a once weekly placebo injection (in fulfilment of post-authorisation measure (PAM) (MEA 004)). As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 3.1) are updated accordingly. In addition, the MAH took the opportunity to update the wording of the existing indication in section 4.1 of the SmPC and to implement a minor change in section 5.1 of the SmPC, in the glycaemic control summary subsection based on the results from the dulaglutide study as add-on to sodium-glucose co-transporter 2 (SGLT2) inhibitor therapy which was assessed as part of variation II/25 concluded in April 2018

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

5.3.14. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0017

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include a new indication in adult patients with chronic rhinosinusitis with nasal polyposis. 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

5.3.15. [Fosnetupitant, Netupitant, palonosetron - AKYNZEO \(CAP\) - EMEA/H/C/003728/X/0018](#)

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Extension application to introduce a new pharmaceutical form 'powder for concentrate for solution for infusion' and a new strength for the fixed combination of fosnetupitant (pro-drug of netupitant)/palonosetron of 235 mg/0.25 mg, to be administered intravenously (new route of administration). The RMP (version 2.4) is updated accordingly

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

5.3.16. [Idelalisib - ZYDELIG \(CAP\) - EMEA/H/C/003843/II/0047](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report for study 101-09 (listed as a category 1 study in Annex II and the RMP): a phase 2 study to assess the efficacy and safety of idelalisib in subjects with indolent B-cell non-Hodgkin lymphomas refractory to rituximab and alkylating agents. This submission is an Annex II post-authorisation measure (ANX 002) and a category 1 commitment in the RMP. This submission also includes an update to the product information

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

5.3.17. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/X/0062](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension application to introduce a solution for injection as a new pharmaceutical form, 120 mg as a new strength and subcutaneous use as a new route of administration. The RMP (version 9.1) is updated accordingly

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

5.3.18. [Insulin lispro - HUMALOG \(CAP\) - EMEA/H/C/000088/X/0169](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Extension application. The RMP is updated (version 9.3) accordingly and in line with revision 2 of GVP module V on 'Risk management systems'

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

5.3.19. Insulin lispro - LIPROLOG (CAP) - EMEA/H/C/000393/X/0130

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Extension application. The RMP is updated (version 9.3) accordingly and in line with revision 2 of GVP module V on 'Risk management systems'

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

5.3.20. Interferon beta-1a - REBIF (CAP) - EMEA/H/C/000136/II/0137/G

Applicant: Merck Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.3, 4.6 and 5.3 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries; 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles (in fulfilment of MEA 043.2 and MEA 039). The package leaflet is updated accordingly. The RMP (version 10.0) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

5.3.21. Interferon beta-1b - BETAFERON (CAP) - EMEA/H/C/000081/II/0124/G

Applicant: Bayer AG

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries; 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles (in fulfilment of MEA 024.2 and MEA 021). The package leaflet is updated accordingly. The RMP (version 4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

5.3.22. Interferon beta-1b - EXTAVIA (CAP) - EMEA/H/C/000933/II/0096/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries; 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles (in fulfilment of MEA 022.2 and MEA 019). The package leaflet is updated accordingly. The RMP (version 4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

5.3.23. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0107, Orphan

Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Extension of indication to include Revlimid (lenalidomide) in combination with rituximab for the treatment of adult patients with previously treated follicular lymphoma or marginal zone lymphoma. 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 36.2) are updated accordingly

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

5.3.24. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/II/0049

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Updated of section 4.8 of the SmPC with safety data from study 109: a phase 3, double blind, placebo controlled, parallel group study to evaluate the efficacy and safety of lumacaftor in combination with ivacaftor in subjects aged 6 through 11 years with cystic fibrosis (CF), homozygous for the deletion of phenylalanine in position 508 of the cystic fibrosis transmembrane conductance regulator (F508del-CFTR) mutation; and study 011 Part B (study 011B): a phase 3, open-label study to evaluate the pharmacokinetics, safety, and tolerability of lumacaftor in combination with ivacaftor in subjects 6 through 11 years of age with CF, homozygous for the F508del-CFTR mutation (receiving lumacaftor 200 mg in fixed-dose combination with ivacaftor 250 mg orally q12h for 24 weeks). The RMP (version 7.0) is updated accordingly

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

5.3.25. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/II/0060

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.1, 4.2, 4.3, 4.4, 4.8 and 4.9 of the SmPC in order to update the safety information on benign or malignant neoplasia based on the EU registry study: the Ipsen global safety database and based on a literature review. The package leaflet and the RMP (version 11) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.26. Moroctocog alfa - REFACTO AF (CAP) - EMEA/H/C/000232/II/0151

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.8 and 5.1 of the SmPC based on the final results from study 3082B2-313 (B1831001) (listed as a category 3 study in the RMP): an open-label study to evaluate prophylaxis treatment, and to characterize the efficacy, safety, and pharmacokinetics of b-domain deleted recombinant factor VIII albumin free (moroctocog alfa [AF_CC]) in children with haemophilia A (in fulfilment of MEA 116). The RMP (version 13.0) is updated accordingly. In addition, the SmPC is brought in line with revision 3 of the 'Guideline on core SmPC for human plasma derived and recombinant coagulation factor VIII products' (EMA/CHMP/BPWP/1619/1999 rev. 3)

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

5.3.27. Nusinersen - SPINRAZA (CAP) - EMEA/H/C/004312/II/0014, Orphan

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study SM202 (EMBRACE or CS7) (listed as a category 3 study in the RMP): a phase 2, randomised, double-blind, sham-procedure-controlled study to assess the safety and tolerability and explore the efficacy of nusinersen (ISIS 396443 (BIIB058)) administered intrathecally in subjects with spinal muscular atrophy who are not eligible to participate in study ISIS 396443-CS3B: a phase 3, randomized, double-blind, sham-procedure controlled study to assess the clinical efficacy and safety of nusinersen administered intrathecally in patients with infantile-onset spinal muscular atrophy; or study ISIS 396443-CS4: a phase 3, randomized, double-blind, sham-procedure controlled study to assess the clinical efficacy and safety of nusinersen administered intrathecally in patients with later-onset spinal muscular atrophy; due to age at screening and/or survival motor neuron 2 (SMN2) copy number. The RMP (version 10.1) is updated accordingly

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

5.3.28. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0029

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to reflect the outcome of study D5160C00035 (listed as a category 3 study in the RMP): an open-label, phase 1 study to assess the pharmacokinetics, safety and tolerability of osimertinib following a single oral 80 mg dose to patients with advanced solid tumours and normal renal function or severe renal impairment. The RMP (version 13) is updated accordingly

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

5.3.29. Pegfilgrastim - UDENYCA (CAP) - EMEA/H/C/004413/II/0003

Applicant: ERA Consulting GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.6 of the SmPC to amend the safety information based on feasibility data regarding the pregnancy and lactation registry (listed as a category 3 study in the RMP). The package leaflet and the RMP (version 1.5) are updated accordingly

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

5.3.30. Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/II/0052/G

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries; 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles (in fulfilment of MEA 08.2 and MEA 002). The package leaflet is updated accordingly. The RMP (version 4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

5.3.31. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0065

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include Keytruda (pembrolizumab) as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) chemotherapy, first-line treatment of

recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) in adults; based on the results from KEYNOTE-048: a randomized, multicentre, open-label phase 3 study investigating pembrolizumab, or pembrolizumab plus platinum plus 5-FU chemotherapy versus platinum plus 5-FU plus cetuximab in subjects with first-line recurrent or metastatic HNSCC. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 22.1) are updated accordingly

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

5.3.32. Pemetrexed - PEMETREXED FRESENIUS KABI (CAP) - EMEA/H/C/003895/X/0009

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Ghania Chamouni

Scope: Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/mL. The RMP (version 2.0) is updated accordingly

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

5.3.33. Propranolol - HEMANGIOL (CAP) - EMEA/H/C/002621/II/0019

Applicant: Pierre Fabre Dermatologie

PRAC Rapporteur: Eva Segovia

Scope: Submission of the results of a drug utilisation study (DUS) performed in Germany and France to evaluate off-label use and effectiveness of risk minimisation measures (RMM) in a real-life clinical setting (in fulfilment of MEA 002). As a consequence, the package leaflet is updated to strengthen the warning on hypoglycaemia and bronchospasm. The RMP (version 3.1) is updated accordingly. In addition, the MAH took the opportunity to introduce some editorial changes in section 4.4 of the SmPC as well as changes in the package leaflet in accordance with the latest quality review document (QRD) template (version 10.0)

Action: For adoption of PRAC Assessment Report

5.3.34. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0076

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of moderately severe to severe non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated with. The package leaflet and the RMP (version 19.0) are updated accordingly

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

5.3.35. Regadenoson - RAPISCAN (CAP) - EMEA/H/C/001176/II/0034/G

Applicant: GE Healthcare AS

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 4.8 of the SmPC regarding myocardial ischaemia (myocardial infarction, ventricular arrhythmias and cardiac arrest) based on a review of the safety database and company core safety datasheet (CCDS) update; 2) update of sections 4.4, 4.5, 4.8, 4.9 and 5.1 of the SmPC regarding co-administration with methylxanthine due to the risk of seizure and hypersensitivity including anaphylaxis based on a review of the safety database and CCDS update; 3) update of section 5.1 of the SmPC regarding the use of regadenoson in patients with inadequate stress test based on results from study 3606-CL-3004: a phase 3b, open-label, parallel group, randomized, multicentre study to assess regadenoson administration following an inadequate exercise stress test as compared to regadenoson alone for myocardial perfusion imaging (MPI) using single photon emission computed tomography (SPECT); and CCDS update. The RMP (version 11.1) is updated accordingly (in fulfilment of LEG 016)

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

5.3.36. Rituximab - MABTHERA (CAP) – EMEA/H/C/000165/II/0168

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Extension of indication in previously untreated, advanced stage paediatric B-cell Non-Hodgkin's lymphoma (B-NHL). The RMP (version 21.0) is updated accordingly

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

5.3.37. Rituximab - RIXATHON (CAP) - EMEA/H/C/003903/WS1599/0020; RIXIMYO (CAP) - EMEA/H/C/004729/WS1599/0020

Applicant: Sandoz GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of the final report from study GP13-301 (listed as a category 3 study in the RMP): a randomized, controlled double-blind phase 3 trial to compare the efficacy, safety and pharmacokinetics of Rixathon/Riximyo (GP2013 – rituximab biosimilars) plus cyclophosphamide, vincristine, prednisone vs. MabThera (rituximab) plus cyclophosphamide, vincristine, prednisone, followed by Rixathon/Riximyo (GP2013 - rituximab biosimilars) or MabThera (rituximab) maintenance therapy in patients with previously untreated advanced stage follicular lymphoma. The RMP (version 4.0) is updated accordingly

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

5.3.38. Sodium zirconium cyclosilicate - LOKELMA (CAP) - EMEA/H/C/004029/II/0013

Applicant: AstraZeneca AB

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the clinical information based on final results from study DIALIZE: a Phase 3b, multicentre, prospective, randomised, double-blind, placebo-controlled study to reduce incidence of pre-dialysis hyperkalaemia with sodium zirconium cyclosilicate. The package leaflet, labelling

and the RMP (version 2.1) are updated accordingly. In addition, the MAH took the opportunity to reflect information on sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'. Furthermore, minor editorial changes were introduced in the package leaflet

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

5.3.39. [Tofacitinib - XELJANZ \(CAP\) - EMEA/H/C/004214/X/0012](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension application to introduce a new pharmaceutical form (prolonged-release tablet) associated with a new strength (11 mg), and presented in pack sizes of 28, 30, 90 and 91 tablets. The extension of indication includes a change in pharmacokinetics. The RMP (version 4.0) is updated accordingly

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

5.3.40. [Trastuzumab emtansine - KADCYLA \(CAP\) - EMEA/H/C/002389/II/0045](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Extension of indication to include the adjuvant treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive early breast cancer. 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 9.0) are updated accordingly. In addition, the MAH took the opportunity to introduce some editorial changes

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

5.3.41. [Trastuzumab emtansine - KADCYLA \(CAP\) - EMEA/H/C/002389/II/0048/G](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 4.8 of the SmPC in order to update the safety information on the risk of left ventricular dysfunction (LVD) based on the final results from study BO39807 (listed as a category 3 study in the RMP): an observational study of cardiac events in patients with epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer who have a left ventricular ejection fraction (LVEF) between 40%-49% prior to initiating treatment with Kadcykla (trastuzumab emtansine). The RMP (version 10.0) is updated accordingly; 2) submission of the final report from study BO28408 (listed as a category 3 study in the RMP): a randomised, multicentre, open-label, two-arm, phase 3 neoadjuvant study evaluating the efficacy and safety of trastuzumab emtansine plus pertuzumab compared with chemotherapy plus trastuzumab and pertuzumab for patients with HER2-positive breast cancer

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

5.3.42. Trifluridine, tipiracil - LONSURF (CAP) - EMEA/H/C/003897/II/0016

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with severe renal impairment based on final results from study TO-TAS-102-107: a phase 1, open-label study to evaluate the safety, tolerability, and pharmacokinetics of trifluridine/tipiracil (TAS-102) in patients with advanced solid tumours and varying degrees of renal impairment. The package leaflet and the RMP (version 6.3) are updated accordingly. In addition, the MAH took the opportunity to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

5.3.43. Turoctocog alfa - NOVOEIGHT (CAP) - EMEA/H/C/002719/II/0030/G

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of submission of: 1) results of study NN7008-3809 (Guardian 4): safety and efficacy of turoctocog alfa in prevention and treatment of bleeds in paediatric previously untreated patients (PUPs) with haemophilia A and; 2) results of study NN7008-4239 (Guardian 9): a multicentre, open-label trial evaluating the pharmacokinetics (PK) of NovoEight (turoctocog alfa) in relation to body mass index (BMI) in subjects with haemophilia A. In addition, the product information is brought in line with revision 3 of the 'Guideline on core SmPC for human plasma derived and recombinant coagulation factor VIII products' (EMA/CHMP/BPWP/1619/1999 rev. 3) and in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'. Sections 2, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC and the package leaflet are updated accordingly. Furthermore, the MAH took the opportunity to introduce some administrative updates in the product information

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

5.3.44. Vemurafenib - ZELBORAF (CAP) - EMEA/H/C/002409/II/0054

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to add information and a precaution regarding concomitant use of strong cytochrome P450 3A4 (CYP3A4) inhibitors based on final results from study GO29475 (MEA-011) (listed as a category 3 study in the RMP): a two-part, phase 1, open-label, multicentre, two-period, one-sequence study to investigate the effect of itraconazole and rifampin on the pharmacokinetic (PK) of vemurafenib at steady state. The package leaflet and the RMP (version 12.0) are updated accordingly. In addition, the package leaflet is updated to reflect information on sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.45. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/II/0035

Applicant: Correvio

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information following updates to the company core safety datasheet (CCDS) based on the results of an integrated safety analysis performed on data of existing clinical studies with a stronger emphasis on treatment-related adverse drug reactions (ADRs) and an incidence rate above one percent. The package leaflet and the RMP (version 7.0) are updated accordingly. In addition, the RMP is updated in line with the results from the completed observational cohort SPECTRUM study (study 6621-049): a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant intravenous (IV) sterile concentrate currently under assessment in variation II/34. Furthermore, the MAH took the opportunity to update sections 4.2, 4.4, 4.6, 4.7, 4.8, 5.1, 5.2, 5.3, 6.4 of the SmPC, Annex II, labelling and package leaflet in order to include editorial changes, to correct typographical errors and to bring the product information in line with the latest quality review of documents (QRD) template (version 10). The package leaflet is also updated in line with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' and the EMA Annex to the EC guideline

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. Albutrepenonacog alfa - IDELVION (CAP) - PSUSA/00010497/201901

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (Δ LNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - ZALMOXIS (CAP) - PSUSA/00010530/201902

Applicant: MolMed S.p.A, ATMP⁵

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

⁵ Advanced therapy medicinal product

Action: For adoption of recommendation to CAT and CHMP

6.1.3. Atazanavir, cobicistat - EVOTAZ (CAP) - PSUSA/00010404/201901

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Axitinib - INLYTA (CAP) - PSUSA/00010022/201901

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Baricitinib - OLUMIANT (CAP) - PSUSA/00010578/201902

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Besilesomab - SCINTIMUN (CAP) - PSUSA/00000385/201901 (with RMP)

Applicant: Cis Bio International

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Bevacizumab - AVASTIN (CAP); MVASI (CAP); ZIRABEV (CAP) - PSUSA/00000403/201902

Applicant(s): Amgen Europe B.V. (Mvasi), Pfizer Europe MA EEIG (Zirabev), Roche Registration GmbH (Avastin)

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. [Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY \(CAP\) - PSUSA/00010695/201902](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. [Brentuximab vedotin - ADCETRIS \(CAP\) - PSUSA/00010039/201902](#)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. [Brexpiprazole - RXULTI \(CAP\) - PSUSA/00010698/201901](#)

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Tatiana Magalova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. [Brimonidine⁶ - MIRVASO \(CAP\) - PSUSA/00010093/201902](#)

Applicant: Galderma International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. [Brivaracetam - BRIVIACT \(CAP\) - PSUSA/00010447/201901](#)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. [Burosumab - CRYSVITA \(CAP\) - PSUSA/00010669/201902](#)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

⁶ Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/201901

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Ceftazidime, avibactam - ZAVICEFTA (CAP) - PSUSA/00010513/201902

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Chlormethine - LEDAGA (CAP) - PSUSA/00010587/201902

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Colistimethate sodium⁷ - COLOBREATHE (CAP) - PSUSA/00009112/201902

Applicant: Teva B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Collagenase clostridium histolyticum⁸ - XIAPEX (CAP) - PSUSA/00000871/201902

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

⁷ Dry inhalation powder only

⁸ Indicated for the treatment of Dupuytren's contracture and treatment of Peyronie's disease

6.1.19. Dapagliflozin, metformin - EBYMECT (CAP); XIGDUO (CAP) - PSUSA/00010294/201901

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Daunorubicin, cytarabine - VYXEOS (CAP) - PSUSA/00010701/201902

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Dexamethasone⁹ - OZURDEX (CAP) - PSUSA/00000985/201901

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated), haemophilus type b conjugate vaccine (adsorbed) - VAXELIS (CAP) - PSUSA/00010469/201904

Applicant: MCM Vaccine B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Dolutegravir – TIVICAY (CAP); dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - PSUSA/00010075/201901

Applicant(s): ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

⁹ Centrally authorised product(s) only, indicated in the treatment of uveitis and macular oedema

6.1.24. Elbasvir, grazoprevir - ZEPATIER (CAP) - PSUSA/00010519/201901

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Elosulfase alfa - VIMIZIM (CAP) - PSUSA/00010218/201902

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Entacapone - COMTAN (CAP); COMTESS (CAP); ENTACAPONE ORION (CAP) - PSUSA/00001223/201901

Applicant(s): Novartis Europharm Limited (Comtan), Orion Corporation (Comtess, Entacapone Orion)

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Eravacycline - XERAVA (CAP) - PSUSA/00010718/201902

Applicant: Tetrphase Pharmaceuticals Ireland Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Etanercept¹⁰ - BENEPALI (CAP); ERELZI (CAP) - PSUSA/00010452/201901

Applicant(s): Samsung Bioepis NL B.V. (Benepali), Sandoz GmbH (Erelzi)

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Etanercept¹¹ - ENBREL (CAP) - PSUSA/00001295/201902

Applicant: Pfizer Europe MA EEIG

¹⁰ Biosimilar product(s) only

¹¹ All except biosimilar product(s)

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. [Evolocumab - REPATHA \(CAP\) - PSUSA/00010405/201901](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. [Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR \(CAP\) - PSUSA/00010352/201902](#)

Applicant: Chiesi Farmaceutici S.p.A., ATPM¹²

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.32. [Fenofibrate, simvastatin - CHOLIB \(CAP\) - PSUSA/00010096/201902](#)

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. [Ferric maltol - FERACCRU \(CAP\) - PSUSA/00010476/201902](#)

Applicant: Norgine B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. [Florbetaben \(¹⁸F\) - NEURACEQ \(CAP\) - PSUSA/00010094/201902](#)

Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹² Advanced therapy medicinal product

6.1.35. Fluticasone, salmeterol¹³ - AERIVIO SPIROMAX (CAP); AIREXAR SPIROMAX (CAP) - PSUSA/00010531/201902

Applicant(s): Teva B.V.

PRAC Rapporteur: Iliaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Glecaprevir, pibrentasvir - MAVIRET (CAP) - PSUSA/00010620/201901

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Glycerol phenylbutyrate - RAVICTI (CAP) - PSUSA/00010454/201901

Applicant: Immedica Pharma AB

PRAC Rapporteur: Iliaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Hydrocortisone¹⁴ - ALKINDI (CAP) - PSUSA/00010674/201902

Applicant: Diurnal Europe BV

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Ingenol mebutate - PICATO (CAP) - PSUSA/00010035/201901

Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Lanadelumab - TAKHZYRO (CAP) - PSUSA/00010743/201902

Applicant: Shire Pharmaceuticals Ireland Limited

¹³ Centrally authorised products only

¹⁴ Centrally authorised product(s) for adrenal insufficiency, paediatric use only

PRAC Rapporteur: Kirsti Villikka
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.41. Lenvatinib - KISPLYX (CAP); LENVIMA (CAP) - PSUSA/00010380/201902

Applicant(s): Eisai GmbH
PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.42. Mercaptamine¹⁵ - CYSTADROPS (CAP) - PSUSA/00010574/201901

Applicant: Recordati Rare Diseases
PRAC Rapporteur: Eva Segovia
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.43. Metreleptin - MYALEPTA (CAP) - PSUSA/00010700/201901

Applicant: Aegerion Pharmaceuticals B.V.
PRAC Rapporteur: Adam Przybylkowski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.44. Modified vaccinia Ankara virus - IMVANEX (CAP) - PSUSA/00010119/201901

Applicant: Bavarian Nordic A/S
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.45. Nilotinib - TASIGNA (CAP) - PSUSA/00002162/201901

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Hans Christian Siersted
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

¹⁵ Indicated for treatment of corneal cystine

6.1.46. Nitisinone - ORFADIN (CAP) - PSUSA/00002169/201902

Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Ospemifene - SENSHIO (CAP) - PSUSA/00010340/201902

Applicant: Shionogi B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Paclitaxel albumin - ABRAXANE (CAP) - PSUSA/00010123/201901

Applicant: Celgene Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Palbociclib - IBRANCE (CAP) - PSUSA/00010544/201902

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Patisiran - ONPATTRO (CAP) - PSUSA/00010715/201902

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Pegfilgrastim - FULPHILA (CAP); NEULASTA (CAP); PELGRAZ (CAP); PELMEG (CAP); UDENYCA (CAP); ZIEXTENZO (CAP) - PSUSA/00002326/201901

Applicant(s): Accord Healthcare S.L.U. (Pelgraz), Amgen Europe B.V. (Neulasta), Cinfa Biotech S.L. (Pelmeg), ERA Consulting GmbH (Udenyca), Mylan S.A.S (Fulphila), Sandoz GmbH (Ziextenzo)

PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.52. Perflutren - LUMINITY (CAP); OPTISON (CAP) - PSUSA/00002350/201812

Applicant(s): GE Healthcare AS (Optison), Lantheus EU Limited (Luminality)
PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.53. Phenylephrine, ketorolac - OMIDRIA (CAP) - PSUSA/00010419/201901

Applicant: Omeros Ireland Limited
PRAC Rapporteur: Jan Neuhauser
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.54. Pirfenidone - ESBRIET (CAP) - PSUSA/00002435/201902

Applicant: Roche Registration GmbH
PRAC Rapporteur: Rhea Fitzgerald
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.55. Pomalidomide - IMNOVID (CAP) - PSUSA/00010127/201902

Applicant: Celgene Europe BV
PRAC Rapporteur: Eva Segovia
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.56. Reslizumab - CINQAERO (CAP) - PSUSA/00010523/201902

Applicant: Teva B.V.
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.57. [Rivastigmine - EXELON \(CAP\); PROMETAX \(CAP\); RIVASTIGMINE 1A PHARMA \(CAP\); RIVASTIGMINE HEXAL \(CAP\); RIVASTIGMINE SANDOZ \(CAP\) - PSUSA/00002654/201901](#)

Applicant(s): 1 A Pharma GmbH (Rivastigmine 1A Pharma), Hexal AG (Rivastigmine Hexal), Novartis Europharm Limited (Exelon, Prometax), Sandoz GmbH (Rivastigmine Sandoz)

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. [Ruxolitinib - JAKAVI \(CAP\) - PSUSA/00010015/201902](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.59. [Safinamide - XADAGO \(CAP\) - PSUSA/00010356/201902](#)

Applicant: Zambon S.p.A.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.60. [Samarium \(¹⁵³Sm\) lexidronam - QUADRAMET \(CAP\) - PSUSA/00002682/201902](#)

Applicant: Cis Bio International

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.61. [Silodosin - SILODYX \(CAP\); UROREC \(CAP\) - PSUSA/00002701/201901](#)

Applicant(s): Recordati Ireland Ltd

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.62. [Simoctocog alfa - NUWIQ \(CAP\); VIHUMA \(CAP\) - PSUSA/00010276/201901](#)

Applicant(s): Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.63. [Sodium phenylbutyrate - AMMONAPS \(CAP\); PHEBURANE \(CAP\) - PSUSA/00002758/201812](#)

Applicant(s): Eurocept International B.V. (Pheburane), Immedica Pharma AB (Ammonaps)

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.64. [Sugammadex - BRIDION \(CAP\) - PSUSA/00002799/201901](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.65. [Telotristat - XERMELO \(CAP\) - PSUSA/00010639/201902](#)

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.66. [Tezacaftor, ivacaftor - SYMKEVI \(CAP\) - PSUSA/00010730/201902](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.67. [Tisagenlecleucel - KYMRIAH \(CAP\) - PSUSA/00010702/201902](#)

Applicant: Novartis Europharm Limited, ATMP¹⁶

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

¹⁶ Advanced therapy medicinal product

6.1.68. Tivozanib - FOTIVDA (CAP) - PSUSA/00010636/201902

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.69. Trastuzumab emtansine - KADCYLA (CAP) - PSUSA/00010136/201902

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.70. Ulipristal acetate¹⁷ - ESMYA (CAP); ULIPRISTAL ACETATE GEDEON RICHTER (CAP) - PSUSA/00009325/201902

Applicant(s): Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.71. Verteporfin - VISUDYNE (CAP) - PSUSA/00003110/201812

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.72. Vismodegib - ERIVEDGE (CAP) - PSUSA/00010140/201901

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.73. Voretigene neparvovec - LUXTURNA (CAP) - PSUSA/00010742/201901

Applicant: Novartis Europharm Limited, ATMP¹⁸

¹⁷ Indicated for treatment of moderate to severe symptoms of uterine fibroids

¹⁸ Advanced therapy medicinal product

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

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

6.2.1. Lenalidomide - LENALIDOMIDE ACCORD (CAP); REVLIMID (CAP); NAP - PSUSA/00001838/201812

Applicant(s): Accord Healthcare S.L.U. (Lenalidomide Accord), Celgene Europe BV (Revlimid), various

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Pregabalin - LYRICA (CAP); PREGABALIN PFIZER (CAP); NAP - PSUSA/00002511/201901

Applicant(s): Pfizer Europe MA EEIG (Lyrica, Pregabalin Pfizer), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Rasagiline - AZILECT (CAP); RASAGILINE RATIOPHARM (CAP); NAP - PSUSA/00002612/201901

Applicant(s): Teva B.V. (Azilect, Rasagiline ratiopharm), various

PRAC Rapporteur: Ana Sofia Diniz Martins

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. 5-fluorouracil¹⁹ (NAP) – PSUSA/00010000/201901

Applicant(s): various

PRAC Lead: Martin Huber

¹⁹ For topical formulation(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Alitretinoin²⁰ (NAP) – PSUSA/00010710/201901

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Ambrosia artemisiifolia^{21 22 23} (NAP) – PSUSA/00010693/201901

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Amino acid combinations^{24 25}(NAP) – PSUSA/00010187/201901

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Amlodipine, losartan (NAP) – PSUSA/00010512/201901

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Benzydamine, cetylpyridine (NAP) – PSUSA/00000378/201901

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

²⁰ For oral use only

²¹ For sublingual use only

²² Medicinal product(s) authorised via decentralised procedure

²³ Allergen for therapy

²⁴ Combinations of pure amino acids or amino acids with mineral compounds/electrolytes only

²⁵ Intravenous (I.V.) formulation(s) only

Action: For adoption of recommendation to CMDh

6.3.7. Bezafibrate (NAP) – PSUSA/00000405/201901

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Biotin (NAP) – PSUSA/00000414/201901

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Bisoprolol, hydrochlorothiazide (NAP) - PSUSA/00000420/201811

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Botulinum neurotoxin type A (150 kD) free from complexing proteins (NAP) - PSUSA/00009084/201812

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Botulinum toxin A (NAP) - PSUSA/00000426/201812

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Botulinum toxin A-haemagglutinin complex (NAP) - PSUSA/00000427/201812

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.13. Bupropion (NAP) - PSUSA/00000461/201812

Applicant(s): various
PRAC Lead: Liana Gross-Martirosyan
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.14. Caffeine, ergotamine (NAP) - PSUSA/00000485/201811

Applicant(s): various
PRAC Lead: Adrien Inoubli
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.15. Camellia sinensis^{26 27} (NAP) - PSUSA/00010569/201812

Applicant(s): various
PRAC Lead: Adam Przybylkowski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.16. Carboplatin (NAP) - PSUSA/00000559/201901

Applicant(s): various
PRAC Lead: Amelia Cupelli
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.17. Ciclosporin²⁸ (NAP) - PSUSA/00000745/201812

Applicant(s): various
PRAC Lead: Maia Uusküla
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

²⁶ Leaf, dry extract refined, derived from *Camellia sinensis*, L. O. Kuntze

²⁷ For topical use only

²⁸ For systemic use only

6.3.18. Dexketoprofen, tramadol (NAP) - PSUSA/00010468/201901

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Flumazenil (NAP) - PSUSA/00001413/201812

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Flunitrazepam (NAP) - PSUSA/00001418/201901

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Hepatitis A vaccine (inactivated, adsorbed) (NAP) - PSUSA/00001596/201901

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Ketoprofen²⁹ (NAP) - PSUSA/00009205/201901

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Landiolol (NAP) - PSUSA/00010570/201902

Applicant(s): various

PRAC Lead: Menno van der Elst

²⁹ For topical use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Niflumic acid (NAP) - PSUSA/00002157/201812

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Pentoxyverine (NAP) - PSUSA/00002345/201812

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Protirelin (NAP) - PSUSA/00009273/201901

Applicant(s): various

PRAC Lead: Jana Lukačšínová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Roxithromycin (NAP) - PSUSA/00002669/201812

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Testosterone³⁰ (NAP) - PSUSA/00010631/201812

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

³⁰ All formulations apart from topical use

6.3.29. Testosterone³¹ (NAP) - PSUSA/00002908/201812

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Zafirlukast³² - PSUSA/00003138/201812

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Fluticasone furoate - AVAMYS (CAP) - EMEA/H/C/000770/LEG 027.1

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to LEG 027 [cumulative review of cases of respiratory, thoracic and mediastinal disorders together with a cumulative review of lower respiratory tract infections, as requested in the conclusions of PSUSA/009154/201804 adopted in December 2018] as per the request for supplementary information (RSI) adopted in May 2019

Action: For adoption of advice to CHMP

6.4.2. Interferon beta-1a - REBIF (CAP) - EMEA/H/C/000136/LEG 044.1

Applicant: Merck Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 044 [detailed justification regarding the decrease of spontaneous reports during the period covered by the PSUSA procedure together with a cumulative review of cases of panniculitis, as requested in the conclusions of periodic single assessment procedure PSUSA/00009198/201805 adopted at the December 2018 PRAC (held on 26-29 November 2018)] as per the conclusions adopted in April 2019

Action: For adoption of advice to CHMP

6.4.3. Lacosamide - VIMPAT (CAP) - EMEA/H/C/000863/LEG 035

Applicant: UCB Pharma S.A.

³¹ For topical use only

³² Last marketing authorisation(s) valid in the EU withdrawn on 26 August 2019

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Cumulative review of cases of metabolic/toxic encephalopathy as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00001816/201808 adopted in April 2019

Action: For adoption of advice to CHMP

6.4.4. Zoledronic acid - ACLASTA (CAP) - EMEA/H/C/000595/LEG 037

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Detailed review on rheumatological/immune-mediated syndrome (RIMS) following intravenous bisphosphonate therapy from pooled controlled clinical studies, non-clinical data and post-marketing cases, as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00009334/201808 adopted in April 2019

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)³³

7.1.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/PSP/S/0079.1

Applicant: Kite Pharma EU B.V., ATMP³⁴

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to PSP/S/0079 [protocol for a long-term, non-interventional study in patients taking Yescarta (axicabtagene ciloleucel) for the treatment of relapsed or refractory diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma to evaluate the safety of patients, including secondary malignancies, cytokine release syndrome (CRS), neurologic events, serious infections, prolonged cytopenias, hypogammaglobulinaemia and pregnancy outcomes in female patients of childbearing potential] as per the request for supplementary information (RSI) adopted in May 2019

Action: For discussion

7.1.2. Dapagliflozin – EDISTRIDE (CAP); FORXIGA (CAP) - EMEA/H/C/PSP/S/0083

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Protocol for a non-interventional PASS: an observational cohort study using existing data sources in European countries to estimate the incidence of diabetic ketoacidosis (DKA) in type 1 diabetes mellitus (T1DM) dapagliflozin users following implementation of risk

³³ In accordance with Article 107n of Directive 2001/83/EC

³⁴ Advanced therapy medicinal product

minimisation measures (RMMs) in Europe, as required in the outcome of the extension of indication procedure on type 1 diabetes mellitus (T1DM) (EMA/H/C/WS1344) finalised in January 2019

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

7.1.3. [Ingenol mebutate – PICATO \(CAP\) - EMA/H/C/PSP/S/0081](#)

Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Protocol for an observational comparative safety study (POCKET) of patients with actinic keratosis in German claims database to evaluate the safety of ingenol mebutate gel treatment

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

7.1.4. [Nonacog beta pegol – REFIXIA \(CAP\) - EMA/H/C/PSA/S/0041](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Amendment to a protocol previously agreed in June 2018 (PSP/S/0059) for a non-interventional PASS in male haemophilia B patients receiving nonacog beta pegol (N9-GP) prophylaxis treatment to investigate safety of N9-GP during long-term routine use

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

7.1.5. [Sotagliflozin – ZYNQUISTA \(CAP\) - EMA/H/C/PSP/S/0084](#)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Protocol for an observational retrospective cohort study using existing data sources on the incidence of diabetic ketoacidosis (DKA) in adult patients with type 1 diabetes mellitus (T1DM) treated with sotagliflozin as an adjunct to insulin versus insulin alone, as required in the outcome of the initial opinion/marketing authorisation (EMA/H/C/004889) finalised in February 2019

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

7.1.6. [Tisagenlecleucel - KYMRIAH \(CAP\) - EMA/H/C/PSP/S/0066.1](#)

Applicant: Novartis Europharm Ltd, ATMP³⁵

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to PSA/S/0066 [protocol for non-interventional study CCTL019B2401 with secondary use of data from two registries conducted by the 'European Society for Blood and Marrow Transplantation' (EBMT) and 'Centre for International Blood and Marrow Transplant Research' (CIBMTR) to evaluate the long term safety of patients

³⁵ Advanced therapy medicinal product

with B lymphocyte malignancies treated with tisagenlecleucel (chimeric antigen receptor (CAR)-T cell therapy) in a real-world setting] as per the request for supplementary information (RSI) adopted in April 2019

Action: For discussion

7.1.7. Vestronidase alfa – MEPSEVII (CAP) - EMEA/H/C/PSP/S/0082

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Eva Segovia

Scope: Protocol for a PASS to obtain long-term data on effectiveness and safety of treatment with Mepsevii (vestronidase alfa) and to characterize the entire mucopolysaccharidosis VII, including variability of clinical manifestation, progression and natural history

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

7.1.8. Volanesoren – WAYLIVRA (CAP) - EMEA/H/C/PSP/S/0080

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Protocol for a multinational observational registry (WAY4001) of patients treated with volanesoren to evaluate the safety on severe thrombocytopenia and bleeding in patients with familial chylomicronemia syndrome (FCS)

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)³⁶

7.2.1. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 002.8

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002.7 [amendment to previously agreed protocol for study 1245.96: an observational cohort study using existing data including urinary tract infection (UTI) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors] as per the request for supplementary information (RSI) adopted in April 2019

Action: For adoption of advice to CHMP

7.2.2. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 003.5

Applicant: Boehringer Ingelheim International GmbH

³⁶ 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

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 003.4 [amendment to previously agreed protocol for study 1245.96: an observational cohort study using existing data including urinary tract infection (UTI) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors] as per the request for supplementary information (RSI) adopted in April 2019

Action: For adoption of advice to CHMP

7.2.3. [Ertugliflozin - STEGLATRO \(CAP\) - EMEA/H/C/004315/MEA 002.1](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002 [protocol for study 8835-062/000: a PASS to assess the risk of diabetic ketoacidosis (DKA) among patients with type 2 diabetes mellitus (T2DM) treated with ertugliflozin compared to patients treated with other antihyperglycemic agents [final study report due date: December 2023]] as per the request for supplementary information (RSI) adopted in March 2019

Action: For adoption of advice to CHMP

7.2.4. [Ertugliflozin, metformin hydrochloride - SEGLUROMET \(CAP\) - EMEA/H/C/004314/MEA 002.1](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002 [protocol for study 8835-062/000: a PASS to assess the risk of diabetic ketoacidosis (DKA) among patients with type 2 diabetes mellitus (T2DM) treated with ertugliflozin compared to patients treated with other antihyperglycemic agents [final study report due date: December 2023]] as per the request for supplementary information (RSI) adopted in March 2019

Action: For adoption of advice to CHMP

7.2.5. [Ertugliflozin, sitagliptin - STEGLUJAN \(CAP\) - EMEA/H/C/004313/MEA 002.1](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002 [protocol for study 8835-062/000: a PASS to assess the risk of diabetic ketoacidosis (DKA) among patients with type 2 diabetes mellitus (T2DM) treated with ertugliflozin compared to patients treated with other antihyperglycemic agents [final study report due date: December 2023]] as per the request for supplementary information (RSI) adopted in March 2019

Action: For adoption of advice to CHMP

7.2.6. Follitropin alfa - OVALEAP (CAP) - EMEA/H/C/002608/MEA 002.5

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for extension to study XM17-WH-50005 (SOFIA): safety of Ovaleap (follitropin alfa) in infertile women undergoing superovulation for assisted reproductive technologies: a multi-national, comparative, prospective, non-interventional, observational cohort study [final clinical study report (CSR) expected in Q1 2021]

Action: For adoption of advice to CHMP

7.2.7. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 002

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol for observational cohort study TV48125-MH-50037: a pregnancy registry assessing pregnancy outcomes in patients treated with Ajovy (fremanezumab) (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.8. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 003

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol for observational cohort study TV48125-MH-50038: a pregnancy database study assessing pregnancy outcomes in patients treated with Ajovy (fremanezumab) (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.9. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 002

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol for study I5Q-MC-B003 (listed as a category 3 study in the RMP): a cohort study to actively monitor exposure to galcanezumab during pregnancy among women with migraine, using administrative (secondary) data and to study the incidence of pregnancy outcomes (including hypertension during pregnancy and pre-eclampsia) among women exposed to galcanezumab during pregnancy in comparison to women receiving other prophylactic migraine medication [final clinical study report (CSR) expected in Q4 2024] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.10. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 003

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol for study I5Q-MC-B002 (listed as a category 3 study in the RMP): galcanezumab European drug utilisation and safety outcomes study to describe, in real-world clinical practice the utilisation of galcanezumab in Europe, and the incidence of important safety outcomes such as serious hypersensitivity and long-term safety including serious cardio-vascular events, and malignancies [final clinical study report (CSR) expected in Q4 2026] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.11. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 004

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol for study I5Q-MC-B001: galcanezumab US drug utilisation and safety outcomes study to describe, in real-world clinical practice, the utilisation of galcanezumab in the US, and the incidence of important safety outcomes such as serious hypersensitivity and long-term safety including serious cardiovascular events, and malignancies final clinical study report (CSR) expected in Q4 2026] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.12. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/MEA 009.3

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Martin Huber

Scope: Amendment to a protocol previously agreed in November 2015 for a PASS: linaclotide safety study assessing the complications of diarrhoea and associated risk factors in selected European populations with irritable bowel syndrome with constipation (IBS-C) for Constella (linaclotide) 290µg capsules

Action: For adoption of advice to CHMP

7.2.13. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.1

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 003 [protocol for study M-14745-40: European psoriasis registry to collect long-term safety data for tildrakizumab and to further characterise the long-term safety profile of tildrakizumab in the treatment of psoriasis under conditions of routine clinical practice (from initial MAA/opinion)] as per the request for supplementary information (RSI) adopted in April 2019

Action: For adoption of advice to CHMP

7.2.14. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 045.4

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA-045.3 [protocol for study RRA-20745: a PASS to investigate the long-term safety in adult patients with moderately to severely active Crohn's disease] as per the request for supplementary information (RSI) adopted in April 2019

Action: For adoption of advice to CHMP

7.2.15. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.5

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: MAH response to MEA 002.4 [amendment to protocol (version 3.0) for study P16-562: a prospective observational study to assess the long term safety profile of venetoclax in a Swedish cohort of chronic lymphocytic leukaemia (CLL) patients [final clinical study report (CSR) planned in December 2025]] as adopted in June 2019

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)³⁷

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)³⁸

7.4.1. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0081

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study RA0022 from the British Society for Rheumatology Biologics Register (BSRBR) (listed as a category 3 study in the RMP): a UK registry which aims to monitor the long term safety of tumour necrosis factor-alfa (TNF- α) inhibitor drugs and other targeted therapies in rheumatoid arthritis patients; together with the interim report from study RA0020 from the German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) (listed as a category 3 study in the RMP): a long-term observational cohort study of the safety and effectiveness of biologic agent in rheumatoid arthritis (RA)

Action: For adoption of PRAC Assessment Report

³⁷ In accordance with Article 107p-q of Directive 2001/83/EC

³⁸ 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

7.4.2. [Desloratadine - AERIUS \(CAP\) - EMEA/H/C/000313/WS1655/0091; AZOMYR \(CAP\) - EMEA/H/C/000310/WS1655/0095; NEOCLARITYN \(CAP\) - EMEA/H/C/000314/WS1655/0089](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study EUPAS15038 (listed as a category 3 study in the RMP): a non-interventional non-imposed PASS study designed to assess the potential risk of desloratadine exposure on seizures, supraventricular tachycardia, and atrial fibrillation or flutter

Action: For adoption of PRAC Assessment Report

7.4.3. [Dexamethasone - OZURDEX \(CAP\) - EMEA/H/C/001140/II/0035](#)

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final report from study CMO-EPI-EYE-0522 (listed as a category 3 study in the RMP): an observational, cross-sectional study conducted in France, Germany, Spain, and the UK aiming at assessing the effectiveness of the educational material provided to treating physicians

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

7.4.4. [Nalmefene - SELINCRO \(CAP\) - EMEA/H/C/002583/II/0025](#)

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Martin Huber

Scope: Submission of the final study reports for: 1) study 15649A: use of Selincro (nalmefene) in European databases, a cohort design using longitudinal electronic medical records or claims databases; 2) study 14910A: a non-interventional multi-country prospective cohort study to investigate the pattern of use of Selincro (nalmefene) and frequency of selected adverse reactions in routine clinical practice

Action: For adoption of PRAC Assessment Report

7.4.5. [Teriflunomide - AUBAGIO \(CAP\) - EMEA/H/C/002514/II/0025](#)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Submission of the final survey reports (listed as a category 3 study in the RMP) for patients and healthcare professionals (HCPs) to assess the effectiveness of the education materials. As part of the submission, the MAH proposes a revised patient card

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. Acridinium - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/ANX 001.6

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Second interim report for study D6560R00004, formerly M/34273/44, (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of acridinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients in the UK. This is a sub-study report addressing the heart failure component of the PASS programme. It also includes stroke and acute myocardial infarction (AMI) incidence rate descriptive analysis

Action: For adoption of advice to CHMP

7.5.2. Acridinium - EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/ANX 001.6

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Second interim report for study D6560R00004 (formerly M/34273/44) (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of acridinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients in the UK. This is a sub-study report addressing the heart failure component of the PASS programme. It also includes stroke and acute myocardial infarction (AMI) incidence rate descriptive analysis

Action: For adoption of advice to CHMP

7.5.3. Acridinium, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP) - EMEA/H/C/003969/ANX 003.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Second interim report for study D6560R00004 (formerly M/34273/44) (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of acridinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients in the UK. This is a sub-study report addressing the heart failure component of the PASS programme. It also includes stroke and acute myocardial infarction (AMI) incidence rate descriptive analysis

Action: For adoption of advice to CHMP

7.5.4. Acridinium, formoterol fumarate dihydrate - DUAKLIR GENUAIR (CAP) - EMEA/H/C/003745/ANX 003.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Second interim report for study D6560R00004 (formerly M/34273/44) (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of acridinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients in the UK. This is a sub-study report addressing the heart failure component of the PASS programme. It also includes stroke and acute myocardial infarction (AMI) incidence rate descriptive analysis

Action: For adoption of advice to CHMP

7.5.5. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/MEA 001.5

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 001.4 [fourth annual interim report for EuroSIDA PASS study 201177 (listed as a category 3 study in the RMP): a prospective observational cohort study in patients receiving dolutegravir to investigate the risk of hypersensitivity reactions (HSR), hepatotoxicity and serious rash (division of acquired immune deficiency syndrome (DAIDS) grading scale category 3 or 4] as per the request for supplementary information (RSI) adopted in May 2019

Action: For adoption of advice to CHMP

7.5.6. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/MEA 007.5

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 007.4 [fourth annual interim report for EuroSIDA PASS study 201177 (listed as a category 3 study in the RMP): a prospective observational cohort study in patients receiving dolutegravir to investigate the risk of hypersensitivity reactions (HSR), hepatotoxicity and serious rash (division of acquired immune deficiency syndrome (DAIDS) grading scale category 3 or 4] as per the request for supplementary information (RSI) adopted in May 2019

Action: For adoption of advice to CHMP

7.5.7. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 002.9

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: First interim report for study 1245.96: an observational cohort study using existing data assessing the risks of acute liver injury, acute kidney injury and chronic kidney disease, severe complications of urinary tract infection, genital infection, and diabetic ketoacidosis in patients with type 2 diabetes mellitus (T2DM) treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors [final clinical study report (CSR)

expected in Q3 2021]

Action: For adoption of advice to CHMP

7.5.8. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 003.6

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: First interim report for study 1245.96: an observational cohort study using existing data assessing the risks of acute liver injury, acute kidney injury and chronic kidney disease, severe complications of urinary tract infection, genital infection, and diabetic ketoacidosis in patients with type 2 diabetes mellitus (T2DM) treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors [final clinical study report (CSR) expected in Q3 2021]

Action: For adoption of advice to CHMP

7.5.9. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 026.7

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fourth progress report for study MK-8259-013, the ulcerative colitis (UC) Nordic registry: a non-interventional observational longitudinal PASS of Simponi (golimumab) in the treatment of UC using Nordic national health registries

Action: For adoption of advice to CHMP

7.5.10. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/MEA 005.3

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: First annual progress report for a drug utilisation study (DUS) of Intuniv (guanfacine extended release) in European countries: a non-imposed, non-interventional, multi-country DUS using retrospective database analysis (DUS-database: EUPAS18735) and a prescriber survey (DUS-survey: EUPAS18739) (version 1.0)

Action: For adoption of advice to CHMP

7.5.11. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/MEA 015.3

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

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

Action: For adoption of advice to CHMP

7.5.12. [Infliximab - INFLECTRA \(CAP\) - EMEA/H/C/002778/MEA 007.5](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual safety and efficacy interim analysis report for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra (infliximab) in patients with rheumatoid arthritis (EU and Korea) [final clinical study report (CSR) expected: May 2026]

Action: For adoption of advice to CHMP

7.5.13. [Infliximab - INFLECTRA \(CAP\) - EMEA/H/C/002778/MEA 010.5](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual safety and efficacy interim analysis report for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra (infliximab) in patients with Crohn's disease (CD), and ulcerative colitis (UC) (EU and Korea) [final clinical study report (CSR) expected: May 2026]

Action: For adoption of advice to CHMP

7.5.14. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/MEA 007.5](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual safety and efficacy interim analysis report for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Remsima (infliximab) in patients with rheumatoid arthritis (EU and Korea) [final clinical study report (CSR) expected: May 2026]

Action: For adoption of advice to CHMP

7.5.15. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/MEA 010.5](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual safety and efficacy interim analysis report for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Remsima (infliximab) in patients with Crohn's disease (CD), and ulcerative colitis (UC) (EU and Korea) [final clinical study report (CSR) expected: May 2026]

Action: For adoption of advice to CHMP

7.5.16. [Nivolumab - OPDIVO \(CAP\) - EMEA/H/C/003985/MEA 021](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Interim clinical study report for study CA209835 (listed as a category 3 study in the RMP): a registry study to analyse transplant-related complications after an allogeneic haematopoietic stem cell transplantation (HCT), among patients with classical Hodgkin lymphoma (cHL) who were previously treated with nivolumab (from variation II/12)

Action: For adoption of advice to CHMP

7.5.17. [Octocog alfa - KOVALTRY \(CAP\) - EMEA/H/C/003825/MEA 005.1](#)

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual interim results 2018 for epidemiological study 15689: an evaluation of adverse events of special interest (AESI) in the PEDiatric NETwork (PedNet) haemophilia registry (from MA/opinion)

Action: For adoption of advice to CHMP

7.5.18. [Ospemifene - SENSHIO \(CAP\) - EMEA/H/C/002780/ANX 001.7](#)

Applicant: Shionogi B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Fourth annual interim report for a PASS (ENCEPP/SDPP/8585) (listed as a category 1 study in Annex II and the RMP): an observational retrospective cohort study of ospemifene utilising existing databases in Germany, Italy, Spain, and the United States to evaluate the incidence of venous thromboembolism and other adverse events in vulvar and vaginal atrophy (VVA) patients treated with ospemifene as compared to: 1) patients newly prescribed selective oestrogen receptor modulators (SERM) for oestrogen-deficiency conditions or breast cancer prevention and; 2) the incidence in untreated VVA patients [final report expected in February 2021]

Action: For adoption of advice to CHMP

7.5.19. [Roflumilast - DAXAS \(CAP\) - EMEA/H/C/001179/ANX 002.8](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Third interim report for PASS D7120R00003 (previously RO-2455-403-RD): a long-term post-marketing observational study exploring the safety of roflumilast in the treatment of chronic obstructive pulmonary disease (COPD), combined data results from Sweden, Germany and the US (Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product') [final clinical study report (CSR) expected in March 2021]

Action: For adoption of advice to CHMP

7.5.20. [Sacubitril, valsartan - ENTRESTO \(CAP\) - EMEA/H/C/004062/MEA 004.6](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Amendment to protocol previously agreed in March 2017 for study LCZ696B2015 (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of Entresto/Neparvis (sacubitril/valsartan) together with MAH's response to MEA 004.5 as per the request for supplementary information (RSI) adopted in June 2019

Action: For adoption of advice to CHMP

7.5.21. [Sacubitril, valsartan - NEPARVIS \(CAP\) - EMEA/H/C/004343/MEA 003.3](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Amendment to protocol previously agreed in March 2017 for study LCZ696B2015 (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of Entresto/Neparvis (sacubitril/valsartan) together with MAH's response to MEA 004.5 as per the request for supplementary information (RSI) adopted in June 2019

Action: For adoption of advice to CHMP

7.5.22. [Ustekinumab - STELARA \(CAP\) - EMEA/H/C/000958/MEA 022.17](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 022.16 [Eighth annual report for study C0168Z03 (PSOLAR: PSoriasis Longitudinal Assessment and Registry): an international prospective cohort study/registry programme designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics] as per the request for supplementary information (RSI) adopted in April 2019

Action: For adoption of advice to CHMP

7.5.23. [Vonicog alfa - VEYVONDI \(CAP\) - EMEA/H/C/004454/MEA 001.2](#)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study VON (BAX0111) VWF-500 COL (also called ATHN-9 study) (listed as a category 3 study in the RMP): a real world safety and effectiveness study of factor replacement for clinically severe von Willebrand disease (VWD) [final report due date: 30/06/2022] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.5.24. Voriconazole - VFEND (CAP) - EMEA/H/C/000387/MEA 091.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 091.2 [second interim report for non-interventional study A1501103: an active safety surveillance programme to monitor selected events in patients with long-term voriconazole use] as per the request for supplementary information (RSI) adopted in March 2019

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.7

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: First feasibility assessment report for study NB-451: an observational retrospective study based on secondary data analysis using existing databases, in order to evaluate the potential population of patients or prescriptions in each database and confirm the ability to use each database for the drug utilisation study (DUS) of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) in selected European countries to describe the demographic and baseline characteristics of users of Mysimba (naltrexone hydrochloride/bupropion hydrochloride)

Action: For adoption of advice to CHMP

7.6.2. Prucalopride - RESOLOR (CAP) - EMEA/H/C/001012/REC 022.1

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to REC 022 [report from the FDA³⁹ on study SPD555-802: a retrospective cohort (observational) study measuring the incidence of major adverse cardiovascular events (MACE; non-fatal acute myocardial infarction, non-fatal stroke, or in-hospital cardiovascular death) in five European data sources, as requested in the conclusions of variation II/42 concluded in September 2018] as per the request for supplementary information (RSI) adopted in May 2019

Action: For adoption of advice to CHMP

7.6.3. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005.1

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

³⁹ US Food & Drug Administration

Scope: Proposal for amendment to previously agreed protocols in September 2014 for: 1) pregnancy registry OBS12751 (international): an international pregnancy exposure registry of women with multiple sclerosis (MS) exposed to Aubagio (teriflunomide) and; 2) pregnancy registry OBS13499 (US/CA): teriflunomide pregnancy outcome exposure registry: a 'teratology information specialists (OTIS)' autoimmune diseases in pregnancy project. The purpose of this position paper is to describe the challenges in achieving enrolment targets, to outline the actions implemented to date to increase enrolment, to provide statistical considerations

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Cholic acid - KOLBAM (CAP) - EMEA/H/C/002081/S/0029 (without RMP)

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Agni Kapou

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0018 (without RMP)

Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/R/0026 (without RMP)

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Ciclosporin - IKERVIS (CAP) - EMEA/H/C/002066/R/0017 (without RMP)

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Clopidogrel - CLOPIDOGREL RATIOPHARM (CAP) - EMEA/H/C/004006/R/0014 (with RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Dalbavancin - XYDALBA (CAP) - EMEA/H/C/002840/R/0028 (without RMP)

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/R/0021 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. [Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA \(CAP\) - EMEA/H/C/003687/R/0033 \(without RMP\)](#)

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. [Nonacog gamma - RIXUBIS \(CAP\) - EMEA/H/C/003771/R/0029 \(with RMP\)](#)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. [Oritavancin - ORBACTIV \(CAP\) - EMEA/H/C/003785/R/0027 \(without RMP\)](#)

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. [Paliperidone - TREVICTA \(CAP\) - EMEA/H/C/004066/R/0022 \(with RMP\)](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. [Sevelamer carbonate - SEVELAMER CARBONATE WINTHROP \(CAP\) - EMEA/H/C/003971/R/0022 \(with RMP\)](#)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Laurence de Fays

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. [Tedizolid phosphate - SIVEXTRO \(CAP\) - EMEA/H/C/002846/R/0031 \(without RMP\)](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

- 10.1.1. Interferon beta-1a – AVONEX (CAP) - EMEA/H/C/000102/II/0182/G, REBIF (CAP) - EMEA/H/C/000136/II/0137/G;
Interferon beta-1b - BETAFERON (CAP) - EMEA/H/C/000081/II/0124/G; EXTAVIA (CAP) - EMEA/H/C/000933/II/0096/G
peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/II/0052/G

Applicant(s): Bayer AG (Betaferon), Biogen Netherland (Avonex, Plegridy), Merck Europe B.V. (Rebif), Novartis Europharm Limited (Extavia)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: PRAC consultation on individual variations for (peg)interferon beta-containing products on use in pregnancy, namely: grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries; 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles (in fulfilment of MEA 024.2 and MEA 021). The package leaflet is updated accordingly. The RMP (version

4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of advice to CHMP

See also under 5.3.20. 5.3.21. 5.3.22. and 5.3.30.

10.1.2. Dimethyl fumarate – TECFIDERA (CAP) - EMEA/H/C/002601/II/0063

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: PRAC consultation on an update of sections 4.4 and 4.8 of the SmPC to reflect progressive multifocal leukoencephalopathy (PML) in the setting of mild lymphopenia based on data submitted in the ongoing PSUSA/00010143/201903 due for recommendation at the November 2019 PRAC meeting. The package leaflet is updated accordingly. Additionally, the Product Information has been updated in line with the quality review of documents (QRD) template (version 10.1)

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

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

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. 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, Ulla Wändel Liminga, Menno van der Elst, Tatiana Magálová, Ghania Chamouni, Jan Neuhauser

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Working Party with Patients' and Consumers' Organisations (PCWP) and Working Party with Healthcare Professionals' Organisations (HCPWP) - work plan 2019-2020

Action: For adoption

12.4. Cooperation within the EU regulatory network

12.4.1. PRAC strategic review and learning meeting (SRLM) under the Finnish presidency of the European Union (EU) Council – Helsinki, Finland, 22-23 October 2019 - agenda

PRAC lead: Kirsti Villikka, Kimmo Jaakkola

Action: For discussion

12.4.2. PRAC strategic review and learning meeting (SRLM) under the Romanian presidency of the European Union (EU) Council -Bucharest, Romania, 22-23 May 2019 - report

PRAC lead: Roxana Stroe, Alexandra Spurni

Action: For discussion

12.5. Cooperation with International Regulators

12.5.1. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)-E2D on 'post-approval safety

data management' reflection paper - pharmacoepidemiology discussion group (PEpi-DG): call for nominations

Action: For adoption

12.5.2. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)-E19 on 'optimisation of safety data collection' – draft guideline

Action: For adoption

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

12.7. PRAC work plan

12.7.1. PRAC work plan 2019 – mid-year report

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q2 2019 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q2 2019

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.11.2. Signal management - monitoring EudraVigilance data by MAHs – experience from the pilot period

Action: For discussion

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. EMA relocation to new building, Amsterdam, the Netherlands – update on planned timelines

Action: For discussion

12.20.2. Good Pharmacovigilance Practice (GVP) Guideline on product or population specific considerations III: pregnancy and breastfeeding – key areas for discussion following comments on the draft guideline

PRAC lead: Ulla Wändel Liminga

Action: For discussion

12.20.3. Patient registry initiative and cross-committee task force on registries – call for additional volunteers

Action: For discussion

12.20.4. Process for nomination of Rapporteurs for referral procedures – revised principles

Action: For discussion

13. Any other business

14. Explanatory notes

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

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures

(Items 2 and 3 of the PRAC agenda)

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

Signals assessment and prioritisation

(Item 4 of the PRAC agenda)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.

The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.

The evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

Risk Management Plans (RMPs)

(Item 5 of the PRAC agenda)

The RMP describes what is known and not known about the side effects of a medicine and states how these risks will be prevented or minimised in patients. It also includes plans for studies and other activities to gain more knowledge about the safety of the medicine and risk factors for developing side effects.

RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available.

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC agenda)

A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.

PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC agenda)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC agenda)

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

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