13 January 2020
EMA/PRAC/645087/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 13-16 January 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

13 January 2020, 13:00 – 19:30, room 2/D

14 January 2020, 08:30 – 19:30, room 2/D

15 January 2020, 08:30 – 19:30, room 2/D

16 January 2020, 08:30 – 16:00, room 2/D

Organisational, regulatory and methodological matters (ORGAM)

30 January 2020, 09:00 – 12:00, room 1/F, 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 on 13-16 January 2020. See (current) January 2020 PRAC minutes (to be published post February 2020 PRAC meeting).

1.2. Agenda of the meeting on 13-16 January 2020

Action: For adoption

1.3. Minutes of the previous meeting on 25-28 November 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. Ingenol mebutate - PICATO (CAP) - EMEA/H/A-20/1489

Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Adam Przybylkowski; PRAC Co-rapporteur: Adrien Inoubli

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)

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

3.4.1. Estradiol[2] (NAP) - EMEA/H/A-31/1482

Applicant(s): various

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

Scope: Re-examination under Article 32 of Directive 2001/83/EC for the review of the benefit-risk balance of medicinal product(s) containing estradiol 0.01% for topical use following notification by the European Commission (EC) of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption of a recommendation to CMDh

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Baricitinib – OLUMIANT (CAP)

Applicant: Eli Lilly Nederland B.V.

[1] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[2] 0.01%, topical use only
[3] Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

PRAC Rapporteur: Adam Przybylkowski

Scope: Signal of diverticulitis

Action: For adoption of PRAC recommendation

EPITT 19496 – New signal

Lead Member State(s): PL

4.1.2. Desogestrel (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of suppressed lactation

Action: For adoption of PRAC recommendation

EPITT 19504 – New signal

Lead Member State(s): SE

4.1.3. Dupilumab – DUPIXENT (CAP)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of corneal disorders

Action: For adoption of PRAC recommendation

EPITT 19509 – New signal

Lead Member State(s): FI

4.1.4. Mirtazapine (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of amnesia

Action: For adoption of PRAC recommendation

EPITT 19506 – New signal

Lead Member State(s): NL

4.1.5. Nivolumab – OPDIVO (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of lichen sclerosus

Action: For adoption of PRAC recommendation

EPITT 19505 – New signal

Lead Member State(s): DE

4.1.6. Sertraline (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of microscopic colitis

Action: For adoption of PRAC recommendation

EPITT 19513 – New signal

Lead Member State(s): NL

4.2. New signals detected from other sources

4.2.1. Dabrafenib – TAFINLAR (CAP); trametinib – MEKINIST (CAP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: To be appointed

Scope: Signal of disseminated intravascular coagulation (DIC)

Action: For adoption of PRAC recommendation

EPITT 19510 – New signal

Lead Member State(s): NO, SE

4.2.2. Fluoroquinolones: cinoxacin (NAP); ciprofloxacin (NAP); ciprofloxacin, dexamethasone (NAP); ciprofloxacin, fluocinolone (NAP); ciprofloxacin, hydrocortisone (NAP); delafloxacin – QUOFENIX (CAP); levofloxacin – QUINSAIR (CAP); lomefloxacin (NAP); moxifloxacin (NAP); nadifloxacin (NAP); norfloxacin (NAP); ofloxacin (NAP); ofloxacin, dexamethasone (NAP); ozenoxacin (NAP); pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP)

Applicant(s): A. Menarini Industrie Farmaceutiche Riunite (Quofenix), Chiesi Farmaceutici S.p.A. (Quinsair), various

PRAC Rapporteur: To be appointed

Scope: Signal of heart valve regurgitation

Action: For adoption of PRAC recommendation

EPITT 19522 – New signal

Lead Member State(s): DE, DK, ES, FR, IT, HR

4.3. Signals follow-up and prioritisation

4.3.1. Abiraterone – ZYTIGA (CAP) - EMEA/H/C/002321/SDA/022; 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: Eva Segovia

Scope: Signal of interaction with sulphonylureas leading to hypoglycaemia

Action: For adoption of PRAC recommendation

EPITT 19445 – Follow-up to September 2019

4.3.2. Adalimumab – AMGEVITA (CAP); HALIMATOZ (CAP); HEFIYA (CAP); HULIO (CAP); HUMIRA (CAP) - EMEA/H/C/000481/SDA/115; HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP)

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Humira), Amgen Europe B.V. (Amgevita), Fresenius Kabi Deutschland GmbH (Idacio), 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 – Follow-up to September 2019

4.3.3. Anastrozole (NAP)

Applicant(s): various

PRAC Rapporteur: Zane Neikena

Scope: Signal of hallucinations

Action: For adoption of PRAC recommendation

EPITT 19449 – Follow-up to September 2019

4.3.4. Dipeptidyl peptidase-4 (DPP4) inhibitors: alogliptin - VIPIDIA (CAP) - EMEA/H/C/002182/SDA/012; alogliptin, metformin hydrochloride - VIPDOMET (CAP) - EMEA/H/C/002654/SDA/009; alogliptin, pioglitazone - INCRESYNC (CAP) - EMEA/H/C/002178/SDA/009; linagliptin - TRAJENTA (CAP) - EMEA/H/C/002110/SDA/019; saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/SDA/044; saxagliptin, dapagliflozin - QTERN (CAP) - EMEA/H/C/004057/SDA/007; sxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/SDA/019; sitagliptin – JANUVIA (CAP) - EMEA/H/C/000722/SDA/039, RISTABEN (CAP) - EMEA/H/C/001234/SDA/017, TESAVEL (CAP) - EMEA/H/C/000910/SDA/033, XELEVIA (CAP) - EMEA/H/C/000762/SDA/038; NAP; sitagliptin, ertugliflozin – STEGLUJAN (CAP);

sitagliptin, metformin – EFFICIB (CAP); JANUMET (CAP); VELMETIA (CAP);NAP; vildagliptin - GALVUS (CAP) - EMEA/H/C/000771/SDA/048, JALRA (CAP) - EMEA/H/C/001048/SDA/032, XILIARX (CAP) - EMEA/H/C/001051/SDA/032; vildagliptin, metformin hydrochloride - EUCREAS (CAP) - EMEA/H/C/000807/SDA/026, ICANDRA (CAP) - EMEA/H/C/001050/SDA/024, ZOMARIST (CAP) - EMEA/H/C/001049/SDA/024; NAP

Applicant(s): AstraZeneca AB (Kombogzyle, Onglyza, Qtern), Boehringer Ingelheim International GmbH (Trajenta), Merck Sharp & Dohme B.V. (Efficib, Janumet, Januvia, Ristaben, Steglujan, Tesavel, Velmetia, Xelevia), Takeda Pharma A/S (Incresync, Vipidia, Vipdomet), Novartis Europharm Limited (Eucreas, Galvus, Icandra, Jalra, Xiliarx, Zomarist), various

PRAC Rapporteur: Menno van der Elst

Scope: Signal of rhabdomyolysis

Action: For adoption of PRAC recommendation

EPITT 19466 – Follow-up to September 2019

4.3.5. Golimumab – SIMPONI (CAP) – EMEA/H/C/000992/SDA/035

Applicant(s): Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of inflammatory myopathy

Action: For adoption of PRAC recommendation

EPITT 19460 – Follow-up to September 2019

4.3.6. Hormone replacement therapy (HRT): chlorotrianisene (NAP); conjugated estrogens (NAP); conjugated estrogens, bazedoxifene - DUAVIVE (CAP); dienestrol (NAP); diethylstilbestrol (NAP); estradiol (NAP); estradiol, norethisterone (NAP); estriol (NAP); estrone (NAP); ethinylestradiol (NAP); methallenestril (NAP); moxestrol (NAP); promestriene (NAP); tibolone (NAP)

Applicant(s): Pfizer Europe MA EEIG (Duavive), various

PRAC Rapporteur: Menno van der Elst

Scope: New information on the known risk of breast cancer

Action: For adoption of PRAC recommendation

EPITT 19482 – Follow-up to October 2019

4.3.7. Immune checkpoint inhibitors: atezolizumab – TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/018; avelumab – BAVENCIO (CAP) - EMEA/H/C/004338/SDA/005; cemiplimab – LIBTAYO (CAP) EMEA/H/C/004844/SDA/004; durvalumab – IMFINZI (CAP) EMEA/H/C/004771/SDA/003; ipilimumab – YERVOY (CAP) EMEA/H/C/002213/SDA/039; nivolumab – OPDIVO (CAP) EMEA/H/C/003985/SDA/039; pembrolizumab - KEYTRUDA (CAP) EMEA/H/C/003820/SDA/024

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: Brigitte Keller-Stanislawski

Scope: Signal of tuberculosis

Action: For adoption of PRAC recommendation

EPITT 19464 – Follow-up to September 2019

4.3.8. Prasugrel – EFIENT (CAP) - EMEA/H/C/000984/SDA/035, PRASUGREL MYLAN (CAP), NAP

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

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of severe cutaneous adverse reactions (SCARs)

Action: For adoption of PRAC recommendation

EPITT 19463 – Follow-up to September 2019

4.3.9. Sacubitril, valsartan – ENTRESTO (CAP) - EMEA/H/C/004062/SDA/009; NEPARVIS (CAP) - EMEA/H/C/004343/SDA/004

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of ventricular arrhythmia

Action: For adoption of PRAC recommendation

EPITT 19448 – Follow-up to September 2019

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Budesonide, formoterol fumarate dihydrate - EMEA/H/C/004882

Scope: Treatment of asthma and chronic obstructive pulmonary disease (COPD)

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

5.1.2. Budesonide, glycopyrronium, formoterol fumarate dihydrate - EMEA/H/C/004983

Scope: Maintenance treatment in adult patients with moderate to very severe chronic obstructive pulmonary disease (COPD)

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

5.1.3. Bulevirtide - EMEA/H/C/004854, Orphan

Applicant: MYR GmbH

Scope (accelerated assessment): Treatment of chronic hepatitis delta virus (HDV) infection in adult patients with compensated liver disease

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

5.1.4. Elexacaftor, tezacaftor, ivacaftor - EMEA/H/C/005269, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

Scope (accelerated assessment): Treatment of cystic fibrosis

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

5.1.5. Indacaterol, glycopyrronium, mometasone - EMEA/H/C/005061

Scope: Treatment of asthma and reduction of asthma exacerbations

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

5.1.6. Indacaterol, glycopyrronium, mometasone - EMEA/H/C/005518

Scope: Treatment of asthma and reduction of asthma exacerbations

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

5.1.7. Indacaterol, mometasone furoate - EMEA/H/C/005067

Scope: Treatment of asthma

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

5.1.8. Pretomanid - EMEA/H/C/005167, Orphan

Applicant: FGK Representative Service GmbH

Scope: Treatment of tuberculosis

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. Abacavir - ZIAGEN (CAP) - EMEA/H/C/000252/WS1713/0109; abacavir, lamivudine - KIVEXA (CAP) - EMEA/H/C/000581/WS1713/0083; dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/WS1713/0075; lamivudine, abacavir, zidovudine - TRIZIVIR (CAP) - EMEA/H/C/000338/WS1713/0115

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of updated RMPs (version 2.0 for Kivexa, Trizivir and Ziagen; version 17.0 for Triumeq) in order to remove the additional risk minimisation measure (aRMM) on the education materials for healthcare professionals on abacavir hypersensitivity. Annex II is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.2. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/II/0050/G

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 5.0) in order to amend the list of safety concerns to remove 'cataract (in the context of very low 'low-density lipoprotein cholesterol' (LDL-C))' as an important potential risk; 'long-term use (>5years)' and 'clinical impact of very low LDL-C for extended period of time' as missing information. As a consequence, the following additional pharmacovigilance activities (listed as category 3 studies in the RMP) are removed from the RMP: 1) study R727-CL-1609: a long term safety study of Praluent (alirocumab) in patients with heterozygous familial hypercholesterolemia or with non-familial hypercholesterolemia at high and very high cardiovascular risk and previously enrolled in the neurocognitive function trial (MEA 016); 2) study OBS14697: a drug utilisation study (DUS) of alirocumab in Europe to assess the effectiveness of the dosing recommendation to avoid very low low-density lipoprotein (LDL)-C levels (MEA 019); 3) study ALIROC07997: a PASS using healthcare databases, in order to monitor the safety of Praluent (alirocumab) in patients affected with the human immunodeficiency virus (HIV) (MEA 017) based on a review of data since the marketing authorisation (MA) was granted including the first interim report for study OBS14697 (in fulfilment of MEA 019.4)

Action: For adoption of PRAC Assessment Report

5.2.3. Dexamethasone - OZURDEX (CAP) - EMEA/H/C/001140/II/0037

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Eva Segovia

Scope: Submission of an updated RMP (version 9.0) in order to reflect increased knowledge of the medicinal product and bring it in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.4. Docetaxel - DOCETAXEL ZENTIVA (CAP) - EMEA/H/C/000808/II/0061

Applicant: Zentiva, k.s.

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of an updated RMP (version 1.1) in order to revise the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and to complete Part II modules

Action: For adoption of PRAC Assessment Report

5.2.5. Docetaxel - TAXOTERE (CAP) - EMEA/H/C/000073/II/0134

Applicant: Aventis Pharma S.A.

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of an updated RMP version 1.1 in order to revise the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and to complete Part II modules

Action: For adoption of PRAC Assessment Report

5.2.6. Follitropin alfa - GONAL-F (CAP) - EMEA/H/C/000071/II/0147

Applicant: Merck Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 2.1) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template), to remove the important identified risks of 'ovarian hyperstimulation syndrome (OHSS)', 'thromboembolic events usually with OHSS', 'hypersensitivity reactions, including anaphylactic reactions', 'asthma aggravated/exacerbation', 'multiple pregnancies' and 'gynecomastia in males'. In addition, the RMP is updated to remove the important potential risks of 'breast cancer', 'other reproductive system cancers', 'ectopic pregnancy' and 'congenital abnormalities'. Finally, the RMP is updated to increase the age from 40 to 42 years for the missing information of 'women older than 40 years'

Action: For adoption of PRAC Assessment Report

5.2.7. Follitropin alfa, lutropin alfa - PERGOVERIS (CAP) - EMEA/H/C/000714/II/0066

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 5.3) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template), to remove the important identified risks of 'ovarian hyperstimulation syndrome (OHSS)', 'thromboembolic events usually with OHSS' and 'hypersensitivity reactions', to remove the important potential risks of 'breast cancer', 'ovarian cancer', 'endometrial cancer', 'congenital anomalies' and 'malignant melanoma'

Action: For adoption of PRAC Assessment Report

5.2.8. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/II/0115

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Submission of an updated RMP (version 12) in order to revise the lists 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

5.2.9. Lacosamide - LACOSAMIDE UCB (CAP) - EMEA/H/C/005243/WS1748/0003; Lacosamide - VIMPAT (CAP) - EMEA/H/C/000863/WS1748/0085

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP in order to change due dates for three studies (listed as a category 3 studies in the RMP): 1) study SP848: an open-label study to determine safety, tolerability and efficacy of long -term oral lacosamide (LCM) as adjunctive therapy in children with epilepsy - from November 2021 to December 2021; 2) study EP0012: an open-label, multicentre extension study to evaluate the long-term safety and efficacy of LCM as adjunctive therapy for uncontrolled primary generalised tonic clonic seizures in subjects with idiopathic generalised epilepsy - from November 2022 to December 2022; 3) study EP0034: a multicentre, open-label, long-term extension study to investigate the efficacy and safety of LCM as adjunctive therapy in paediatric subjects with epilepsy with partial-onset seizures - from May 2024 to August 2024. In addition, the submission includes amendments to the agreed protocols for studies SP848 and EP0034

Action: For adoption of PRAC Assessment Report

5.2.10. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/II/0030

Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: Submission of an updated RMP (version 11.3) as a result of interim analysis and updated final report submission dates for study E7080-G000-307: a multicentre, open-label, randomized, phase 3 trial to compare the efficacy and safety of lenvatinib in combination with everolimus or pembrolizumab versus sunitinib alone in first-line treatment of subjects with advanced renal cell carcinoma (CLEAR). The protocol is also updated to include an interim analysis for profession-free survival and overall survival

Action: For adoption of PRAC Assessment Report

5.2.11. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/II/0050, Orphan

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 9) in order to update the list of safety

concerns, consisting of: 1) deletion of the important identified risk 'occurrence of anti-teduglutide antibodies, cross reactivity with glucagon-like peptide-2 (GLP-2) and occurrence of anti-eosinophil cationic protein (ECP) antibodies'; 2) deletion of the important potential risk 'increased C-reactive protein (CRP)'; 3) renaming of important identified risks for clarity to 'biliary events', 'pancreatic events' and 'intestinal polyps'. In addition, the submission includes a minor amendment to a protocol for study TED-R-13-002: an international short bowel syndrome registry: a prospective, long-term observational cohort study of patients with short bowel syndrome, as requested by PRAC in procedure PSA/S/0040 adopted in July 2019

Action: For adoption of PRAC Assessment Report

5.2.12. Temsirolimus - TORISEL (CAP) - EMEA/H/C/000799/II/0078

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 4.0) in order to remove the following safety concerns: 'risk of cardiovascular events in patients with coexisting cardiovascular conditions' and 'reproductive toxicity' as missing information and to bring it in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

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

5.3.1. Adalimumab - HALIMATOZ (CAP) - EMEA/H/C/004866/X/0013

Applicant: Sandoz GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to add a new strength of 20 mg (20 mg/0.4 mL) for Halimatoz (adalimumab) solution for injection in pre-filled syringe. The RMP (version 2.0) is updated accordingly. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IA/11 finalised in March 2019 and June 2019 respectively) and to align the product information with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.2. Adalimumab - HEFIYA (CAP) - EMEA/H/C/004865/X/0013

Applicant: Sandoz GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to add a new strength of 20 mg (20 mg/0.4 mL) for Hefiya (adalimumab) solution for injection in pre-filled syringe. The RMP (version 2.0) is updated accordingly. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IA/11 finalised in March 2019 and June 2019 respectively) and to align the product information with the latest quality review of

documents (QRD) template (version 10.1)

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

5.3.3. Adalimumab - HYRIMOZ (CAP) - EMEA/H/C/004320/X/0013

Applicant: Sandoz GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to add a new strength of 20 mg (20 mg/0.4 mL) for Hyrimoz (adalimumab) solution for injection in pre-filled syringe. The RMP (version 2.0) is updated accordingly. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IA/11 finalised in March 2019 and June 2019 respectively) and to align the product information with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.4. Albutrepenonacog alfa - IDELVION (CAP) - EMEA/H/C/003955/X/0035, Orphan

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Extension application to add a new strength of 3,500 IU (700 IU/mL) for albutrepenonacog alfa powder and solvent for solution for injection. The RMP (version 3.1) is updated accordingly

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

5.3.5. Anakinra - KINERET (CAP) - EMEA/H/C/000363/II/0070

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Hans Christian Siersted

Scope: Extension of indication to include the treatment of familial Mediterranean fever (FMF) to be given in combination with colchicine, if appropriate. As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The package leaflet and the RMP (version 5.0) are updated accordingly

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

5.3.6. 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

5.3.7. 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. Binimetinib - MEKTOVI (CAP) - EMEA/H/C/004579/WS1695/0007; encorafenib - BRAFTOVI (CAP) - EMEA/H/C/004580/WS1695/0008

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include encorafenib in combination with binimetinib and cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, who have received prior systemic therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.9. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/II/0010/G, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of adults with X-linked hypophosphataemia (XLH), and modification of the currently approved indication in children and adolescents, by removing the qualification 'with growing skeletons', in order to include the treatment in all children with radiographic evidence of bone disease. The application provides new week-48 data from study UX023-CL304; a randomized, double-blind, placebo-controlled, phase 3 study with open-label extension to assess the efficacy and safety of KRN23 in adults with XLH. 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 2.0) are updated in

accordance. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.10. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0084/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information following the final results from three studies (listed as category 3 studies in the RMP) namely: 1) study PS0002 (CIMPASI-2): a phase 3, multicentre, randomized, double-blind, parallel-group, study followed by a dose-blind period and open-label follow-up to evaluate the efficacy and safety of certolizumab pegol in subjects with moderate to severe chronic plaque psoriasis; 2) study PS0003 (CIMPACT): a phase 3, multicentre, randomized, double-blind, parallel-group, placebo- and active-controlled study followed by a placebo-controlled maintenance period and open-label follow-up to evaluate the efficacy and safety of certolizumab pegol in subjects with moderate to severe chronic plaque psoriasis; 3) study PS0005 (CIMPASI-1): a phase 3, multicentre, randomized, double-blind, parallel-group, study followed by a dose-blind period and open-label follow-up to evaluate the efficacy and safety of certolizumab pegol in subjects with moderate to severe chronic plaque psoriasis. The RMP (version 16.0) is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.11. Conestat alfa - RUCONEST (CAP) - EMEA/H/C/001223/II/0053/G

Applicant: Pharming Group N.V

PRAC Rapporteur: Jan Neuhauser

Scope: Grouped variations consisting of an extension of indication to include children in the treatment of acute angioedema attacks with hereditary angioedema (HAE) due to C1 esterase inhibitor deficiency, based on the results from study C1 1209: an open-label, phase 2, single arm study to evaluate the safety, immunogenicity, pharmacokinetics and efficacy of recombinant human C1 inhibitor for the treatment of acute attacks in paediatric patients with hereditary angioedema, from 2 up to and including 13 years of age. In addition, final efficacy and safety data from the open label extension (OLE) phases of 1) study C1 1304: a randomised, placebo-controlled, double-blind, multicentre study performed in order to demonstrate the efficacy of recombinant human C1 inhibitor (rhC1INH) at 100 U/kg in patients with HAE with attacks of angioedema; 2) study C1 1205: a randomised, placebo-controlled, double-blind phase 2 study on the safety and efficacy of rhC1INH at doses of 50 and 100U/kg in relieving eligible attacks of angioedema with involvement of sub-mucosal tissues in patients with HAE; and completed study C1 1310: a phase 3, randomized, placebo-controlled trial on rhC1INH relieved symptoms of hereditary angioedema attacks; together with the final results of studies C1 1207 and 3201 concerning prophylactic treatment of HAE patients. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.7, 4.8, 5.1, 5.2 and 5.3 are updated. The package leaflet and the RMP (version 19.0) are

updated accordingly. The RMP is also brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). Furthermore, the MAH requested an extension for the completion of registry study C1 1412: C1 inhibitor treatment registry to assess the safety and immunological profile of Ruconest (conestat alfa) in the treatment of HAE attacks, from March 2020 to June 2022. Finally, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.12. Darunavir,cobicistat - REZOLSTA (CAP) - EMEA/H/C/002819/II/0033

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ilaria Baldelli

Scope: Extension of indication to extend the approved therapeutic indication of Rezolsta (darunavir/cobicistat) to include a new population, namely the adolescent population aged 12 years old and older with a body weight at least 40 kg. 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 6.0) are updated accordingly. The RMP is also brought 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). In addition, the MAH took the opportunity to update section 4.2 of the SmPC in line with recommendations for other human immunodeficiency virus (HIV) products with regards to administration Rezolsta (darunavir/cobicistat) in case of vomiting

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

5.3.13. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0058

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report (CSR) of study 109MS310 (listed as category 3 study in the RMP): an open-label study to assess the effects of Tecfidera (dimethyl fumarate) on lymphocyte subsets in subjects with relapsing remitting multiple sclerosis (RRMS). The RMP (version 10.1) is updated accordingly, includes updates to reflect safety information available until the data lock point (DLP) of 24 January 2019 and in line with revision 2.01 of the guidance on the format of the risk management plan (RMP) accompanying GVP module V on 'Risk management systems'

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

5.3.14. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/WS1756/0025; ROTEAS (CAP) - EMEA/H/C/004339/WS1756/0012

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Adrien Inoubli

Scope: Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the safety information based on final results from the post-authorisation efficacy study DU176b-C-E314: evaluation of edoxaban in anticoagulant naive patients with non-valvular atrial

fibrillation (NVAF) and high creatinine clearance [protocol MEA004]. This is a study to compare the exposure of edoxaban 75 mg once daily dose to edoxaban 60 mg once daily dose in NVAF anticoagulant-naive patients with $CHADS_2$ score of ≥2 and creatinine clearance (CrCL) >100 mL/min treated for up to 12 months. The RMP (version 9.0) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.15. Etravirine - INTELENCE (CAP) - EMEA/H/C/000900/II/0058

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Adrien Inoubli

Scope: Extension of indication in order to include patient population from 2 to 6 years of age based on the 48 week study results from study TMC125-C234/P1090: a phase 1/2, open-label trial to evaluate the safety, tolerability, pharmacokinetics and antiviral activity of etravirine (ETR) in antiretroviral (ARV) treatment-experienced human immunodeficiency virus-1 (HIV-1) infected infants and children, aged ≥2 months to <6 years. 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 13.1) are updated accordingly. The RMP is also brought in line with revision 2 of GVP module V on 'Risk management systems' and revision 2.0.1 of the guidance on the format of RMP in the EU (template) leading to a reclassification of safety concerns. Finally, the MAH took the opportunity to introduce minor updates to the product information

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

5.3.16. Flutemetamol (^{18}F) - VIZAMYL (CAP) - EMEA/H/C/002557/II/0021

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to include information on the possibility of quantitative methodology assessment based on published studies. The RMP (version 2.1) is updated accordingly to introduce a new educational programme and to bring it in line with revision 2.0.1 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

5.3.17. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/X/0004

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Extension application to add a new strength of 100 mg/mL solution for injection in pre-filled syringe for Emgality (galcanezumab) associated with a new indication to include treatment of episodic cluster headache. The RMP (version 1.1) is updated accordingly

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

5.3.18. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0017

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 5.1) are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.19. Insulin aspart - FIASP (CAP) - EMEA/H/C/004046/II/0018/G

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Ilaria Baldelli

Scope: Grouped variations consisting of: 1) introduction of a new container closure system: Pumpcart cartridge to be used with insulin infusion pump systems (EU/1/16/1160/012); 2) introduction of a new multipack presentation of Fiasp (insulin aspart) 100 units/mL PumpCart solution for injection in cartridge (EU/1/16/1160/013). The RMP (version 4.0) is updated accordingly

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

5.3.20. Iron - VELPHORO (CAP) - EMEA/H/C/002705/X/0020/G

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped application consisting of: 1) extension application to add a new pharmaceutical form with a new strength - powder for oral suspension 125 mg, 2) extension of indication to add the use of Velphoro (iron) for the control of serum phosphorus levels in paediatric patients 2 years of age and older with chronic kidney disease (CKD) stages 4-5 (defined by a glomerular filtration rate (GFR) <30 mL/min/1.73 m^2) or with CKD on dialysis, based on the results from study PA-CL-PED-01: an open-label, randomised, active-controlled, parallel group, multicentre, phase 3 study investigating the safety and efficacy of Velphoro (iron) and calcium acetate in paediatric and adolescent CKD patients with hyperphosphataemia. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The package leaflet, labelling and the RMP (version 7.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.21. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/II/0082, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include a new population for Kalydeco (ivacaftor) 150 mg tablets to extend the use to patients with cystic fibrosis (CF) aged 6 years and older and weighing 25 kg or more who have an R117H mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene and for Kalydeco (ivacaftor) granules 75 mg and 50 mg, to add patients with CF aged 12 months and older and weighing 7 kg to less than 25 kg who have an R117H mutation in the CFTR gene. This is based on a clinical trial and literature data, and post-marketing experience with Kalydeco (ivacaftor). As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 8.5) are updated accordingly

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

5.3.22. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/II/0031

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of moderate to severe plaque psoriasis in children from the age of 6 years and adolescents who are candidates for systemic therapy for Taltz (ixekizumab). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated with new safety and efficacy information. The package leaflet and the RMP (version 7.1) 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

5.3.23. Necitumumab - PORTRAZZA (CAP) - EMEA/H/C/003886/II/0017

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Submission of the exploratory biomarker analysis from 4 clinical studies (listed as category 3 studies in the RMP) namely: 1) study I4X-MC-JFCU: a single-arm, multicentre, phase 1b study with an expansion cohort to evaluate safety and efficacy of necitumumab in combination with abemaciclib in treatment of patients with stage IV non-small cell lung cancer (NSCLC); 2) study I4X-MC-JFCQ: an open-label, multicentre, phase 1b study with an expansion cohort to evaluate safety and efficacy of the combination of necitumumab with pembrolizumab in patients with stage IV NSCLC; 3) study I4X-MC-JFCP: a single-arm, multicentre, open-label, phase 2 study of paclitaxel and carboplatin chemotherapy plus necitumumab in the first-line treatment of patients with stage IV squamous NSCLC; 4) study I6A-MC-CBBE: a phase 2 study of the combination of LY3023414 (samotolisib) and necitumumab after first-line chemotherapy for metastatic squamous non-small cell carcinoma of the lung. The RMP (version 8.1) is updated accordingly

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

5.3.24. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0033

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to support the use of Lynparza (olaparib) tablets (100 mg and 150 mg) for the maintenance treatment of germline breast cancer gene (BRCA) mutation (gBRCAm) metastatic pancreatic cancer based on the results from the pivotal phase 3 study POLO: a phase 3, randomised, double blind, placebo controlled, multicentre study of maintenance olaparib monotherapy in patients with gBRCA mutated metastatic pancreatic cancer whose disease has not progressed on first line platinum based chemotherapy. As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The package leaflet and the RMP (version 18) are updated in accordance. In addition, the MAH took the opportunity to update section 4.8 for Lynparza (olaparib) hard capsules (50 mg) to revise the list of adverse drug reactions (ADR) based on a pooled safety data analysis. Furthermore, the product information is brought in line with the latest Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' on sodium content. The MAH also took the opportunity to include some minor editorial changes in the product information

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

5.3.25. Pemetrexed - PEMETREXED ACCORD (CAP) - EMEA/H/C/004072/X/0010

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Ghania Chamouni

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (25 mg/mL solution for infusion). The RMP (version 1.0) is updated accordingly

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

5.3.26. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[4]) - EMEA/H/W/002300/II/0043

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.5 of the SmPC in order to add immunogenicity data following the interim results from study Malaria-073 (listed as a category 3 study in the RMP): a phase 3 randomized, open, controlled study to evaluate the immunogenicity and safety of Mosquirix when administered as a primary vaccination schedule at 6, 7.5 and 9 months-of-age, with or without co-administration of measles and rubella and yellow fever vaccines, to children living in sub-Saharan Africa. The RMP (version 5.1) is updated accordingly. In addition, the Scientific Opinion Holder (SOH) took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

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

Applicant: Roche Registration GmbH

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

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

5.3.28. Rituximab - BLITZIMA (CAP) - EMEA/H/C/004723/WS1724/0029; RITEMVIA (CAP) - EMEA/H/C/004725/WS1724/0029; TRUXIMA (CAP) - EMEA/H/C/004112/WS1724/0032

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of the final report from study CT-P10 3.3 (listed as a category 3 study in the RMP): a phase 3, randomised, parallel-group, active-controlled, double-blind study to demonstrate equivalence of pharmacokinetics and non-inferiority of efficacy for CT-P10 (biosimilar rituximab) in comparison with Rituxan (rituximab), each administered in combination with cyclophosphamide, vincristine, and prednisone (CVP) in patients with advanced follicular lymphoma. The RMP (version 9.1) is updated accordingly and aligned with the safety concerns of MabThera (rituximab)

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

5.3.29. Roflumilast - DAXAS (CAP) - EMEA/H/C/001179/II/0038

Applicant: AstraZeneca AB

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of an updated RMP (version 19) to amend the list of safety concerns and remove additional risk minimisation measures (aRMM) as advised by PRAC in November 2018. In addition, the RMP is brought in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template) leading to a reclassification of safety concerns. As a consequence, Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated. The MAH took the opportunity to introduce minor changes in section 4.4 of SmPC and in the package leaflet in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.30. Saxagliptin, dapagliflozin - QTERN (CAP) - EMEA/H/C/004057/II/0024

Applicant: AstraZeneca AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Update of sections 4.2, 4.4 and 5.1 of the SmPC with information on the glycaemic efficacy and renal safety of dapagliflozin in patients with type 2 diabetes mellitus (T2DM) and moderate renal impairment (chronic kidney disease (CKD) 3A) based on final results from study D1690C00024 (DERIVE) (dapagliflozin): a multicentre, double-blind, placebo-controlled, parallel group, randomised, phase 3 study to evaluate the glycaemic efficacy and renal safety of dapagliflozin in patients with T2DM and CKD 3A who have inadequate

glycaemic control, and to reflect a change in renal cut-off value for saxagliptin. The package leaflet and the RMP (version 4.1) are updated accordingly. In addition, the MAH took the opportunity to update sections 2, 4.8, 5.2 of the SmPC and Annex II to include the required excipient information in relation to sodium levels and lactose following the update to the Annex to the European Commission (EC) guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use', as well as to bring the product information in line with the EMA guidance on 'Compilation of quality review of documents (QRD) decisions on stylistic matters in product information' (EMA/25090/2002 Rev.18)

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

5.3.31. Sonidegib - ODOMZO (CAP) - EMEA/H/C/002839/II/0024

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Željana Margan Koletić

Scope: Submission of the final report of study CLDE225X2116 (listed as a category 3 study in the RMP): an interventional phase 1b/2, open-label, multicentre, dose-finding study to assess the safety and efficacy of the oral combination of LDE225 (sonidegib) and INC424 (ruxolitinib) in subjects with myelofibrosis. The RMP (version 7.1) is updated accordingly

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

5.3.32. Tacrolimus - PROTOPIC (CAP) - EMEA/H/C/000374/II/0083/G

Applicant: LEO Pharma A/S

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC following results from two non-interventional PASS, namely: 1) JOELLE study (listed as a category 3 study in the RMP): a joint European longitudinal lymphoma and skin cancer evaluation; 2) APPLES study (listed as a category 3 study in the RMP): a prospective paediatric longitudinal evaluation to assess the long-term safety of tacrolimus ointment for the treatment of atopic dermatitis. The package leaflet and the RMP (version 15.1) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

See also under 10.1.1.

5.3.33. Trastuzumab - OGIVRI (CAP) - EMEA/H/C/004916/II/0009

Applicant: Mylan S.A.S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final clinical study report for study MYL-Her-3001: a multicentre, double-blind, randomized, parallel-group, phase 3 study of the efficacy and safety of Hercules (trastuzumab Mylan S.A.S) plus taxane versus Herceptin (trastuzumab) plus taxane as first line therapy in patients with epidermal growth factor receptor 2+ (HER2+) metastatic breast cancer) with the final overall survival (OS). The RMP (version 3) is

updated accordingly

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

5.3.34. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/II/0023/G

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include Venclyxto (venetoclax) in combination with an anti-CD20[5] antibody (obinutuzumab) for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL) based on the results of pivotal study CLL14/BO25323:a prospective, open-label, multicentre randomized phase 3 trial to compare the efficacy and safety of a combined regimen of obinutuzumab and venetoclax (GDC-0199/ABT-199) versus obinutuzumab and chlorambucil in previously untreated patients with CLL and coexisting medical conditions. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC are updated. The package leaflet and the RMP (version 5.1) are updated accordingly. Furthermore, section 5.3 of the SmPC is updated based on the 6 month-carcinogenicity mouse study report, supported by the 4 week dose ranging study in mice and embryo-foetal development (EFD) data. The MAH took the opportunity to introduce minor editorial changes throughout the product information (PI)

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

5.3.35. Zoledronic acid - ZOMETA (CAP) - EMEA/H/C/000336/II/0091

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information on osteonecrosis of the jaw (ONJ) based on final results from study CZOL446EUS122 (listed as a category 3 study in the RMP): a non-interventional, prospective, observational, multicentre cohort study to assess the incidence of ONJ in cancer patients with bone metastases starting zoledronic acid treatment. The RMP (version 12) is updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Afamelanotide - SCENESSE (CAP) - PSUSA/00010314/201906

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

[5] B cell differentiation antigen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alectinib - ALECENSA (CAP) - PSUSA/00010581/201907

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Allopurinol, lesinurad - DUZALLO (CAP) - PSUSA/00010704/201906

Applicant: Grunenthal GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/201907

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Belatacept - NULOJIX (CAP) - PSUSA/00000311/201906

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Binimetinib - MEKTOVI (CAP) - PSUSA/00010717/201906

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Blinatumomab - BLINCYTO (CAP) - PSUSA/00010460/201906

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Brexpiprazole - RXULTI (CAP) - PSUSA/00010698/201907

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Tatiana Magalova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Bromfenac - YELLOX (CAP) - PSUSA/00000436/201905 (with RMP)

Applicant: PharmaSwiss Ceska Republika s.r.o

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Budesonide[6] - JORVEZA (CAP) - PSUSA/00010664/201907

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Cenegermin - OXERVATE (CAP) - PSUSA/00010624/201907

Applicant: Dompe farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Cladribine[7] - MAVENCLAD (CAP) - PSUSA/00010634/201907

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[6] Centrally authorised product(s) only
[7] Indicated for the treatment of multiple sclerosis

6.1.13. Dasatinib - SPRYCEL (CAP) - PSUSA/00000935/201906

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Dengue tetravalent vaccine (live, attenuated) - DENGVAXIA (CAP) - PSUSA/00010740/201906

Applicant: Sanofi Pasteur

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Dimethyl fumarate[8] - SKILARENCE (CAP) - PSUSA/00010647/201906

Applicant: Almirall S.A

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Efmoroctocog alfa - ELOCTA (CAP) - PSUSA/00010451/201906

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Elotuzumab - EMPLICITI (CAP) - PSUSA/00010500/201905

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Encorafenib - BRAFTOVI (CAP) - PSUSA/00010719/201906

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

[8] Indicated for the treatment of psoriasis

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Ertugliflozin - STEGLATRO (CAP) - PSUSA/00010682/201906

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Ertugliflozin, metformin - SEGLUROMET (CAP) - PSUSA/00010680/201906

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - PSUSA/00010681/201906

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Fluciclovine (^{18}F) - AXUMIN (CAP) - PSUSA/00010594/201905

Applicant: Blue Earth Diagnostics Ireland Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Galsulfase - NAGLAZYME (CAP) - PSUSA/00001515/201905

Applicant: BioMarin International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Glibenclamide[9] - AMGLIDIA (CAP) - PSUSA/00010690/201905

Applicant: Ammtek

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Human fibrinogen, human thrombin - EVICEL (CAP); TACHOSIL (CAP); VERASEAL (CAP) - PSUSA/00010297/201906

Applicant(s): Omrix Biopharmaceuticals N. V. (Evicel), Takeda Austria GmbH (TachoSil), Instituto Grifols, S.A. (VeraSeal)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Human papillomavirus 9-valent vaccine (recombinant, adsorbed) - GARDASIL 9 (CAP) - PSUSA/00010389/201906

Applicant: MSD Vaccins

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Human papillomavirus vaccine (rDNA) - 4-valent - GARDASIL (CAP) - PSUSA/00001634/201905

Applicant: MSD Vaccins

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Human plasma protease C1 inhibitor - CINRYZE (CAP) - PSUSA/00010104/201906

Applicant: Shire Services BVBA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] Centrally authorised product(s) only

6.1.29. Hydroxycarbamide[10] - SIKLOS (CAP) - PSUSA/00001692/201906

Applicant: Addmedica S.A.S.

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Inotersen - TEGSEDI (CAP) - PSUSA/00010697/201907

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Inotuzumab ozogamicin - BESPONSA (CAP) - PSUSA/00010659/201906

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Levofloxacin[11] - QUINSAIR (CAP) - PSUSA/00010429/201905

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Lonoctocog alfa - AFSTYLA (CAP) - PSUSA/00010559/201907

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - PSUSA/00010643/201906

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

[10] Centrally authorised product(s) only
[11] For inhalation use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Macimorelin - MACIMORELIN AETERNA ZENTARIS (CAP) - PSUSA/00010746/201907

Applicant: Aeterna Zentaris GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Mexiletine[12] - NAMUSCLA (CAP) - PSUSA/00010738/201906

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Migalastat - GALAFOLD (CAP) - PSUSA/00010507/201905

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Nepafenac - NEVANAC (CAP) - PSUSA/00002143/201905

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Nivolumab - OPDIVO (CAP) - PSUSA/00010379/201907 (with RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Centrally authorised product(s) only

6.1.40. Nonacog beta pegol - REFIXIA (CAP) - PSUSA/00010608/201905

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Nonacog gamma - RIXUBIS (CAP) - PSUSA/00010320/201906

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Nusinersen - SPINRAZA (CAP) - PSUSA/00010595/201905

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Obeticholic acid - OCALIVA (CAP) - PSUSA/00010555/201905

Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Opicapone - ONGENTYS (CAP) - PSUSA/00010516/201906

Applicant: Bial - Portela & Cª, S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Pegvaliase - PALYNZIQ (CAP) - PSUSA/00010761/201905

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Pentosan polysulfate sodium[13] - ELMIRON (CAP) - PSUSA/00010614/201906 (with RMP)

Applicant: bene-Arzneimittel GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Peramivir - ALPIVAB (CAP) - PSUSA/00010687/201906

Applicant: BioCryst Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Pertuzumab - PERJETA (CAP) - PSUSA/00010125/201906

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Rucaparib - RUBRACA (CAP) - PSUSA/00010694/201906

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Selexipag - UPTRAVI (CAP) - PSUSA/00010503/201906

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[13] Centrally authorised product(s) only

6.1.51. Semaglutide - OZEMPIC (CAP) - PSUSA/00010671/201905

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - PSUSA/00010524/201906

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/201906

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - PSUSA/00010630/201907

Applicant: CO.DON AG, ATMP[14]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.55. Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/201907

Applicant: Vanda Pharmaceuticals Germany GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Tedizolid phosphate - SIVEXTRO (CAP) - PSUSA/00010369/201906

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Maria del Pilar Rayon

[14] Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.57. Trametinib - MEKINIST (CAP) - PSUSA/00010262/201905

Applicant: Novartis Europharm Limited

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. Venetoclax - VENCLYXTO (CAP) - PSUSA/00010556/201906

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.59. Vonicog alfa - VEYVONDI (CAP) - PSUSA/00010714/201906

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Edotreotide - SOMAKIT TOC (CAP); NAP - PSUSA/00010552/201906

Applicants: Advanced Accelerator Applications (SomaKit TOC), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Naloxone[15] - NYXOID (CAP); NAP - PSUSA/00010657/201905

Applicants: Mundipharma Corporation (Ireland) Limited (Nyxoid), various

PRAC Rapporteur: Liana Gross-Martirosyan

[15] For use in non-medical setting(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Ulipristal[16] - ELLAONE (CAP); NAP - PSUSA/00003074/201905

Applicants: Laboratoire HRA Pharma (ellaOne), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Amsacrine (NAP) - PSUSA/00000199/201906

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Bemiparin (NAP) - PSUSA/00000312/201904

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Bupivacaine (NAP); bupivacaine hydrochloride, epinephrin (NAP) - PSUSA/00010335/201904

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Cidofovir (NAP) - PSUSA/00010558/201906

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

[16] Indicated for female emergency contraception only

Action: For adoption of recommendation to CMDh

6.3.5. Clevidipine (NAP)- PSUSA/00010288/201905

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Fusidic acid[17] (NAP) - PSUSA/00010226/201905

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Human hemin (NAP) - PSUSA/00001629/201905

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Iobitridol (NAP) - PSUSA/00001761/201904

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Isoniazide, rifampicin (NAP) - PSUSA/00001792/201905

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Levomethadone (NAP) - PSUSA/00001855/201905

Applicant(s): various

[17] Systemic use only

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Levonorgestrel (NAP) - PSUSA/00001856/201905

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Macrogol 3350 (NAP) - PSUSA/00001924/201905

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Macrogol 4000, macrogol 4000 combinations[18] (NAP) - PSUSA/00010392/201905

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Measles vaccine (live attenuated) (NAP) - PSUSA/00001938/201905

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Methadone (NAP) - PSUSA/00002004/201905

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[18] Oral use only

6.3.16. Methoxyflurane (NAP) - PSUSA/00010484/201905

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Misoprostol[19] (NAP) - PSUSA/00010353/201905

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Moxifloxacin[20] (NAP) - PSUSA/00009231/201905

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Nicardipine (NAP) - PSUSA/00002149/201905

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Ozenoxacin (NAP) - PSUSA/00010651/201905

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Pholcodine (NAP) - PSUSA/00002396/201905

Applicant(s): various

PRAC Lead: Adrien Inoubli

[19] Gynaecological indication - labour induction
[20] Systemic use

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Sulprostone (NAP) - PSUSA/00002828/201904

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Tirofiban (NAP) - PSUSA/00002974/201905

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Tolperisone (NAP) - PSUSA/00002991/201906

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Treprostinil (NAP) - PSUSA/00003013/201905

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Yohimbine (NAP) - PSUSA/00003136/201905

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/LEG 012

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Detailed review on weight gain as requested in the conclusions of PSUSA/00010075/201901 adopted by PRAC in September 2019

Action: For adoption of advice to CHMP

6.4.2. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/LEG 009

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Detailed review on weight gain as requested in the conclusions of PSUSA/00010075/201901 adopted by PRAC in September 2019

Action: For adoption of advice to CHMP

6.4.3. Dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/LEG 004

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: David Olsen

Scope: Detailed review on weight gain as requested in the conclusions of PSUSA/00010075/201901 adopted by PRAC in September 2019

Action: For adoption of advice to CHMP

6.4.4. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/LEG 030

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Cumulative analysis of cases of hepatic failure and hepatitis B virus (HBV) reactivation as requested in the conclusions of PSUSA/00010301/201811 adopted by PRAC in June 2019

Action: For adoption of advice to CHMP

6.4.5. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/LEG 062

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review of severe cutaneous skin reactions (SCARs) following the conclusions of periodic safety update single assessment procedure PSUSA/00002326/201901 adopted in September 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)[21]

7.1.1. Dapagliflozin – EDISTRIDE (CAP), FORXIGA (CAP) - EMEA/H/C/PSP/S/0083.1

Applicant: AstraZeneca

PRAC Rapporteur: Annika Folin

Scope: MAH's response to PSP/S/0083 [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 minimisation measures (RMMs) in Europe, as required in the outcome of the extension of indication procedure on type 1 diabetes mellitus (T1DM) (EMEA/H/C/WS1344) finalised in January 2019] as per the request for supplementary information (RSI) adopted in September 2019

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

7.1.2. Ingenol mebutate - PICATO (CAP) - EMEA/H/C/PSP/S/0081.1

Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to PSP/S/0081 [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] as per the request for supplementary information (RSI) adopted in June 2019

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

7.1.3. Methylphenidate hydrochloride (NAP) - EMEA/H/N/PSP/S/0064.3

Applicant: MEDICE Arzneimittel Pütter GmbH & Co. KG

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0064.2 [protocol for a multicentre, observational, prospective PASS to evaluate the safety concerns of long-term cardiovascular and psychiatric risks within the adult attention deficit/hyperactivity disorder (ADHD) population taking Medikinet Retard (methylphenidate hydrochloride) according to normal standard clinical practice] as per the request for supplementary information (RSI) adopted in June 2019

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

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

7.1.4. Turoctocog alfa pegol- ESPEROCT (CAP) - EMEA/H/C/PSP/S/0085

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for a multinational, prospective, open labelled, non-controlled, non-interventional post-authorisation study of turoctocog alfa pegol (N8-GP) during long-term routine prophylaxis and treatment of bleeding episodes in patients with haemophilia A

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

7.1.5. Volanesorsen – WAYLIVRA (CAP) - EMEA/H/C/PSP/S/0080.1

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0080 [protocol for a multinational observational registry (WAY4001) of patients treated with volanesorsen to evaluate the safety on severe thrombocytopenia and bleeding in patients with familial chylomicronemia syndrome (FCS)] as per the request for supplementary information (RSI) adopted in September 2019

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[22]

7.2.1. Ciclosporin - VERKAZIA (CAP) - EMEA/H/C/004411/MEA 001.2

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: MAH's response to MEA 001.1 [protocol and feasibility study for a case-control study linked to existing cancer registries to understand the data sources and analytic methods available to quantify the risk of periocular skin cancer, conjunctival or corneal neoplasia in children treated with Verkazia (ciclosporin)] as per the request for supplementary information (RSI) adopted in July 2019

Action: For adoption of advice to CHMP

7.2.2. Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/MEA 001.1

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to MEA 001 [protocol for study CAMG334A2023: a non-interventional study to examine patient characteristics and drug utilisation patterns in migraine patients treated with prophylactic drugs in the Nordic registries [final clinical study report (CSR) expected end of data collection + 1 year]] as per the request for supplementary information (RSI) adopted in July 2019

[22] 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

Action: For adoption of advice to CHMP

7.2.3. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/MEA 027

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Protocol for study EXCEED (listed as a category 3 study in the RMP): a pan-European PASS to assess the risk of pancreatic cancer among type 2 diabetes mellitus (T2DM) patients who initiated exenatide as compared with those who initiated other non-glucagon-like peptide 1 receptor agonists based glucose lowering drugs

Action: For adoption of advice to CHMP

7.2.4. Exenatide - BYETTA (CAP) - EMEA/H/C/000698/MEA 047

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Protocol for study EXCEED (listed as a category 3 study in the RMP): a pan-European PASS to assess the risk of pancreatic cancer among type 2 diabetes mellitus (T2DM) patients who initiated exenatide as compared with those who initiated other non-glucagon-like peptide 1 receptor agonists based glucose lowering drugs

Action: For adoption of advice to CHMP

7.2.5. Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - GARDASIL (CAP) - EMEA/H/C/000703/MEA 086.1

Applicant: MSD Vaccins

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 086 [yearly interim results for study P070 (listed as category 3 study in the RMP): a post-licensure safety study in males to monitor safety signals through a systematic evaluation in a research database] as per the request for supplementary information (RSI) adopted in October 2019

Action: For adoption of advice to CHMP

7.2.6. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/MEA 002.4

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Amendment to protocol previously agreed in January 2019 for study INSLIC08571 (listed as a category 3 study in the RMP): a cross-sectional multinational, multichannel survey conducted among healthcare professionals and patients to measure the effectiveness of Suliqua (insulin glargine/lixisenatide) educational materials set up to evaluate the knowledge and understanding of the key safety messages in the healthcare professional guide and the patient guide

Action: For adoption of advice to CHMP

7.2.7. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/MEA 014.2

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 014.1 [protocol for study E7080-G000-508: an observational study to characterise hepatic related toxicity and overall safety profile in real-life conditions in the EU (Western population) in hepatocellular carcinoma (HCC) patients, including patients with Child-Pugh B] as per the request for supplementary information (RSI) adopted in July 2019

Action: For adoption of advice to CHMP

7.2.8. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/MEA 001.1

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: MAH's response to MEA 001 [protocol for a PASS to characterise the safety of allogeneic haematopoietic stem cell transplantation (HSCT) in patients with cutaneous t-cell lymphoma (CTCL) treated with mogamulizumab [final clinical study report expected in July 2024]] as per the request for supplementary information (RSI) adopted in July 2019

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[23]

7.3.1. Brentuximab vedotin – ADCETRIS (CAP) - EMEA/H/C/PSR/S/0022

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Results for study MA25101: an observational cohort study of the safety of brentuximab vedotin in the treatment of relapsed or refractory CD30+ Hodgkin lymphoma and relapsed or refractory systemic anaplastic large cell lymphoma (sALCL) evaluating the occurrence of serious adverse events (SAEs) and adverse events of special interest (AESIs) and identifying and describing potential risk factors for peripheral neuropathy

Action: For adoption of PRAC Assessment Report

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[24]

7.4.1. Agalsidase beta - FABRAZYME (CAP) - EMEA/H/C/000370/II/0113

Applicant: Genzyme Europe BV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final report from study AGALSC08994 (listed as a category 3 study in the RMP): a post-authorisation study on Fabrazyme (agalsidase beta) home infusion educational materials effectiveness evaluation: a survey of healthcare providers and patients/caregivers. The RMP (version 2.0) is updated accordingly. The RMP is also updated in line with revision 2 of the guidance on the format of RMP in the EU (template) and with information on study AGAL02603: a multicentre, multinational study of the effects of Fabrazyme (agalsidase beta) treatment on lactation and infants and study AGAL19211: the Fabry registry/pregnancy sub-registry

Action: For adoption of PRAC Assessment Report

7.4.2. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0063/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from studies IM103075 and IM103076 (listed as category 3 studies in the RMP). Study IM103075 is a prospective cohort study to assess the association between belatacept use and risk of post-transplant lymphoproliferative disorder (PTLD) in renal transplant recipients in the United States (US). Study IM103076 is a prospective patient registry study to estimate the incidence rates of confirmed PTLD, central nervous system (CNS) PTLD and progressive multifocal leukoencephalopathy (PML) in adult renal transplant recipients treated with belatacept in the US. The RMP (version 17.0) is updated accordingly and includes some administrative updates

Action: For adoption of PRAC Assessment Report

7.4.3. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0034/G, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Submission of the final reports from studies 20150163 and 20150228 (listed as category 3 study in the RMP) assessing the effectiveness of the additional risk minimisation measures (aRMM) for healthcare professionals (study 20150163) and patients/caregivers (study 20150228)

Action: For adoption of PRAC Assessment Report

[24] 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

7.4.4. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0068

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of the final report related to the physician survey (NO6987) conducted for Exjade (deferasirox) to assess the impact of educational materials on the prescribers' awareness of doses and biological monitoring recommendations and to assess the awareness and appropriate use of both formulations (dispersible tablets and film-coated tablets). The RMP (version 17.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. 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

7.4.6. Duloxetine - CYMBALTA (CAP) - EMEA/H/C/000572/WS1755/0083; DULOXETINE LILLY (CAP) - EMEA/H/C/004000/WS1755/0020; XERISTAR (CAP) - EMEA/H/C/000573/WS1755/0086; YENTREVE (CAP) - EMEA/H/C/000545/WS1755/0068

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study FIJ-MC-B059: an observational study to assess foetal outcomes following maternal exposure to duloxetine and the revised final report from study F1J-MC-B057: an observational study to assess maternal and foetal outcomes following exposure to duloxetine

Action: For adoption of PRAC Assessment Report

7.4.7. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/WS1760/0024; ROTEAS (CAP) - EMEA/H/C/004339/WS1760/0011

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final study report from study ETNA-DUS (listed as a category 3 study in the RMP): the edoxaban treatment in routine clinical practice drug utilisation study, a retrospective drug utilisation chart review study to gain insight on how edoxaban is used in real practice, to identify prescription patterns and to measure the effectiveness of the

educational programmes

Action: For adoption of PRAC Assessment Report

7.4.8. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/WS1653/0230; LIFMIOR (CAP) - EMEA/H/C/004167/WS1653/0024

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Submission of the second 5-year report from the British Society for Rheumatology Biologics Register (BSRBR) also referred as study B1801309 (listed as a category 3 study in the RMP). This is a prospective observational cohort study which investigates the long-term outcomes of patients with rheumatoid arthritis treated with etanercept with particular reference to safety

Action: For adoption of PRAC Assessment Report

7.4.9. Rilpivirine - EDURANT (CAP) - EMEA/H/C/002264/II/0037

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final report from study EUPAS5766 in the EuroSIDA cohort (listed as a category 3 study in the RMP) - a drug utilisation study (DUS): an observational cohort study to assess rilpivirine (RPV) utilisation according to the European SmPC. The RMP (version 9.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.10. 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 educational 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. Aclidinium - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/ANX 001.7

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to ANX 001.6 [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 aclidinium 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] as per the request for supplementary information (RSI) adopted in September 2019

Action: For adoption of advice to CHMP

7.5.2. Aclidinium - EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/ANX 001.7

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to ANX 001.6 [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 aclidinium 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] as per the request for supplementary information (RSI) adopted in September 2019

Action: For adoption of advice to CHMP

7.5.3. Aclidinium, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP) - EMEA/H/C/003969/ANX 003.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to ANX 003.3 [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 aclidinium 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] as per the request for supplementary information (RSI) adopted in September 2019

Action: For adoption of advice to CHMP

7.5.4. Aclidinium, formoterol fumarate dihydrate - DUAKLIR GENUAIR (CAP) - EMEA/H/C/003745/ANX 003.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to ANX 003.3 [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 aclidinium 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] as per the request for supplementary information (RSI) adopted in September 2019

Action: For adoption of advice to CHMP

7.5.5. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 080.7

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of advice to CHMP

7.5.6. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.6

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002.5 [four-year interim report for study PTC124-GD-025o-DMD (listed as a category 3 study in the RMP): a post-approval registry observational study exploring the long-term of ataluren safety and effectiveness in usual care setting [final clinical study report (CSR) expected in April 2023]] as per the request for supplementary information (RSI) adopted in July 2019

Action: For adoption of advice to CHMP

7.5.7. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/MEA 010.5

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Sixth interim report for study TMC207TBC4002 (listed as a category 3 study in the RMP): a multi-country prospective multidrug resistant tuberculosis (MDR-TB) patient registry to monitor bedaquiline safety, utilisation, and emergence of resistance

Action: For adoption of advice to CHMP

7.5.8. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 013.4

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study BEL114256/ HGS1006-C1101: a pregnancy register collecting information on pregnancy and live birth outcomes, and following infants for serious infections during the first year of life [final report submission extended from April

2019 to April 2022]

Action: For adoption of advice to CHMP

7.5.9. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/MEA 001.2

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of advice to CHMP

7.5.10. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 003.7

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 003.6 [MAH's response to MEA 003.5 [second interim report for drug utilisation study (DUS) B2311061 on conjugated oestrogens/bazedoxifene (CE/BZA) in the European Union (EU) to describe baseline characteristics and utilisation patterns of EU patients initiating Duavive (CE/BZA) or oestrogen + progestin (E+P) combination hormone replacement therapy (HRT)]] as per the request for supplementary information (RSI) adopted in July 2019

Action: For adoption of advice to CHMP

7.5.11. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/MEA 089.14

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim study report from the Swedish biologics register: Anti-Rheumatic Therapy In Sweden (ARTIS) [final report for ARTIS registry expected in October 2021]

Action: For adoption of advice to CHMP

7.5.12. Ketoconazole - KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/ANX 002.6

Applicant: HRA Pharma Rare Diseases

PRAC Rapporteur: Željana Margan Koletić

Scope: Second interim annual report for a prospective, multi-country, observational registry study to collect clinical information on patients with endogenous Cushing's syndrome exposed to ketoconazole using the existing European registry on Cushing's syndrome (ERCUSYN) to assess drug utilisation pattern and to document the safety (e.g.

hepatotoxicity, QT prolongation) and effectiveness of ketoconazole

Action: For adoption of advice to CHMP

7.5.13. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 001

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study PUMA-NER-6201: an open-Label study

to characterize the incidence and severity of diarrhoea in patients with early stage human epidermal growth factor receptor 2 positive (HER2+) breast cancer treated with neratinib and intensive loperamide prophylaxis, with/without anti-inflammatory treatment (budesonide) and with/without a bile acid sequestrant (colestipol) [final study results expected in March 2021]

Action: For adoption of advice to CHMP

7.5.14. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/ANX 001.8

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

7.5.15. Rotavirus vaccine (live, oral) - ROTARIX (CAP) - EMEA/H/C/000639/MEA 094.1

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual report for study EPI-ROTA-052 BOD EU SUPP (201433) (EuroRotaNet): an observational community-based strain surveillance study to monitor the potential emergence and spread of novel rotavirus strains throughout Europe [study extended until December 2020]

Action: For adoption of advice to CHMP

7.5.16. Sebelipase alfa - KANUMA (CAP) - EMEA/H/C/004004/ANX 001.3

Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fourth interim report for study ALX-LALD-501: a non-interventional, multicentre, prospective disease and clinical outcome registry of patients with lysosomal acid lipase deficiency (LAL-D) to further understand the disease, its progression and any associated complication, and to evaluate the long-term efficacy and safety of Kanuma (sebelipase alfa)

Action: For adoption of advice to CHMP

7.5.17. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.18

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 022.17 [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 September 2019

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Avatrombopag - DOPTELET (CAP) - EMEA/H/C/004722/MEA 002

Applicant: Dova Pharmaceuticals Ireland Limited

PRAC Rapporteur: Eva Segovia

Scope: Feasibility assessment for study AVA-CLD-402: evaluation of the feasibility of conducting a PASS of Doptelet (avatrombopag) in patients with severe chronic liver disease (CLD) and potential utilisation of data from TARGET PharmaSolutions' ongoing observational studies in patients with severe CLD

Action: For adoption of advice to CHMP

7.6.2. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/LEG 028

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ghania Chamouni

Scope: Six-monthly update on the development of multi-dose nasal spray DoseGuard as requested in the conclusions of procedure R/0049 finalised in April 2019

Action: For adoption of advice to CHMP

7.6.3. Lopinavir, ritonavir - KALETRA (CAP) - EMEA/H/C/000368/LEG 121.2

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Adrien Inoubli

Scope: Annual safety review in children aged from 14 days to 2 years as regards to chronic

exposure to propylene glycol and ethanol and toxicity, medication errors and lack of efficacy/resistance in relation to potentially suboptimal pharmacokinetic (PK) parameters

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0019 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0036 (without RMP)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/S/0061 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Metreleptin - MYALEPTA (CAP) - EMEA/H/C/004218/S/0009 (with RMP)

Applicant: Aegerion Pharmaceuticals B.V.

PRAC Rapporteur: Adam Przybylkowski

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. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/R/0004 (with RMP)

Applicant: Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Autologous CD34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin BB305 lentiviral vector encoding the beta-A-T87Q-globin gene - ZYNTEGLO (CAP) - EMEA/H/C/003691/R/0005 (without RMP)

Applicant: bluebird bio (Netherlands) B.V, ATMP[25]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.3. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0041 (without RMP)

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - EMEA/H/C/003963/R/0031 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

[25] Advanced therapy medicinal product

8.2.5. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/R/0016 (without RMP)

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.6. Volanesorsen - WAYLIVRA (CAP) - EMEA/H/C/004538/R/0003 (without RMP)

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Aripiprazole - ARIPIPRAZOLE ZENTIVA (CAP) - EMEA/H/C/003899/R/0012 (with RMP)

Applicant: Zentiva, k.s.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/003794/R/0044 (without RMP)

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Atazanavir, cobicistat - EVOTAZ (CAP) - EMEA/H/C/003904/R/0031 (without RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Bortezomib - BORTEZOMIB ACCORD (CAP) - EMEA/H/C/003984/R/0022 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/R/0044 (with RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Evolocumab - REPATHA (CAP) - EMEA/H/C/003766/R/0040 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Ivabradine - IVABRADINE ANPHARM (CAP) - EMEA/H/C/004187/R/0014 (with RMP)

Applicant: ANPHARM Przedsiebiorstwo Farmaceutyczne S.A.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Lorlatinib - LORVIQUA (CAP) - EMEA/H/C/004646/R/0004 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/R/0081 (without RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Pregabalin - PREGABALIN MYLAN (CAP) - EMEA/H/C/004078/R/0014 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Pregabalin - PREGABALIN MYLAN PHARMA (CAP) - EMEA/H/C/003962/R/0012 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Pregabalin - PREGABALIN SANDOZ (CAP) - EMEA/H/C/004010/R/0012 (with RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Pregabalin - PREGABALIN SANDOZ GMBH (CAP) - EMEA/H/C/004070/R/0013 (with RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.14. Pregabalin - PREGABALIN ZENTIVA (CAP) - EMEA/H/C/003900/R/0021 (with RMP)

Applicant: Zentiva k.s.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.15. Roflumilast - DAXAS (CAP) - EMEA/H/C/001179/R/0039 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.16. Sonidegib - ODOMZO (CAP) - EMEA/H/C/002839/R/0028 (without RMP)

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Željana Margan Koletić

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.17. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/R/0027 (without RMP)

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.18. Voriconazole - VORICONAZOLE HIKMA (CAP) - EMEA/H/C/003737/R/0010 (with RMP)

Applicant: Hikma Farmaceutica (Portugal), S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

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. Tacrolimus - PROTOPIC (CAP) - EMEA/H/C/000374/II/0083/G

Applicant: LEO Pharma A/S

PRAC Rapporteur: Rhea Fitzgerald

Scope: PRAC consultation on a variation updating sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC following results from two non-interventional PASS, namely: 1) JOELLE study (listed as a category 3 study in the RMP): a joint European longitudinal lymphoma and skin cancer evaluation; 2) APPLES study (listed as a category 3 study in the RMP): a prospective paediatric longitudinal evaluation to assess the long-term safety of tacrolimus ointment for the treatment of atopic dermatitis. The package leaflet and the RMP (version 15.1) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

Action: For adoption of advice to CHMP

See also under 5.3.32.

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

11.1.1. Dexamethasone (NAP) - MT/H/0348/II/002

Applicant(s): Panpharma (Dexamethasone Panpharma)

PRAC Lead: John Joseph Borg

Scope: PRAC consultation on a type II variation assessing a proposal to update the product information with pheochromocytoma crisis following a signal detected by the MAH, on request of Malta

Action: For adoption of advice to Member States

11.1.2. Valproate (NAP) and related substances: sodium valproate (NAP), valproate semi-sodium (NAP), valproic acid (NAP), magnesium valproate (NAP), valpromide (NAP)- NL/H/xxxx/WS/0354

Applicant(s): Sanofi (Depakine) on behalf of a consortium

PRAC Lead: Liana Gross-Martirosyan

Scope: PRAC follow-up consultation on a national worksharing variation on existing registries relating to the condition requesting 'MAHs to conduct a PASS preferably based on existing registries to further characterise the foetal anticonvulsant syndrome in children with valproate in utero exposure as compared to other anti-epileptic drugs' imposed in the outcome of the referral procedure for valproate-containing products under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1454) completed in 2018, on request of the Netherlands

Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Valaciclovir (NAP) - CZ/H/PSUFU/00003086/201812

Applicant(s): GlaxoSmithKline (Valtrex, Zelitrex)

PRAC Lead: Jana Lukačišinová

Scope: PRAC consultation on a worksharing PSUR follow-up (PSU FU) procedure on reviews of cases of severe cutaneous reactions, including blister, skin exfoliation and skin erosion, on drug reaction with eosinophilia and systemic symptoms (DRESS) as well as a review of cases of acute kidney injury (AKI) as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure on flecainide (PSUSA/00003086/201812) concluded in July 2019

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC 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

None

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 - report

PRAC lead: Kirsti Villikka, Kimmo Jaakkola

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2020

PRAC lead: Sabine Straus, Martin Huber

Action: For adoption

12.8. Planning and reporting

12.8.1. PRAC workload statistics – Q3 & Q4 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

12.12. 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

None

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/