08 April 2019
EMA/PRAC/219089/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 08-11 April 2019

Chair: Sabine Straus – Vice-Chair: Martin Huber

08 April 2019, 13:00 – 19:30, room 1/C

09 April 2019, 08:30 – 19:30, room 1/C

10 April 2019, 08:30 – 19:30, room 1/C

11 April 2019, 08:30 – 16:00, room 1/C

Organisational, regulatory and methodological matters (ORGAM)

25 April 2019, 09:00 – 12:00, room 6/D, via teleconference

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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Table of contents

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 08-11 April 2019. See April 2019 PRAC minutes (to be published post May 2019 PRAC meeting).

1.2. Agenda of the meeting on 08-11 April 2019

Action: For adoption

1.3. Minutes of the previous meeting on 11-14 March 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

3.1.1. Oestradiol[1] (NAP) - EMEA/H/A-31/1482

Applicant(s): various

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

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

Action: For adoption of a list of questions

[1] 0.01%, topical use only

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Ibrutinib – IMBRUVICA (CAP)

Applicant(s): Janssen-Cilag International

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Signal of ischemic stroke

Action: For adoption of PRAC recommendation

EPITT 19369 – New signal

Lead Member State(s): HR

4.1.2. Pembrolizumab – KEYTRUDA (CAP)

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

PRAC Rapporteur: Menno van der Elst

Scope: Signal of optic neuritis

Action: For adoption of PRAC recommendation

EPITT 19381 – New signal

Lead Member State(s): NL

4.1.3. Perampanel – FYCOMPA (CAP)

Applicant(s): Eisai GmbH

PRAC Rapporteur: Julie Williams

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

[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

Scope: Signal of hepatotoxicity

Action: For adoption of PRAC recommendation

EPITT 19383 – New signal

Lead Member State(s): UK

4.1.4. Ticagrelor – BRILIQUE (CAP)

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Signal of severe cutaneous adverse reactions (SCARs)

Action: For adoption of PRAC recommendation

EPITT 19375 – New signal

Lead Member State(s): NL

4.2. New signals detected from other sources

4.2.1. Benralizumab – FASENRA (CAP)

Applicant(s): AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Signal of pneumonia

Action: For adoption of PRAC recommendation

EPITT 19368 – New signal

Lead Member State(s): NO

4.2.2. Loperamide (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of Brugada syndrome in the context of abuse with loperamide

Action: For adoption of PRAC recommendation

EPITT 19379 – New signal

Lead Member State(s): PL

4.2.3. Omalizumab – XOLAIR (CAP)

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Signal of acquired haemophilia

Action: For adoption of PRAC recommendation

EPITT 19385 – New signal

Lead Member State(s): SE

4.2.4. Teriflunomide – AUBAGIO (CAP)

Applicant(s): Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Signal of psoriasis

Action: For adoption of PRAC recommendation

EPITT 19366 – New signal

Lead Member State(s): DE

4.3. Signals follow-up and prioritisation

4.3.1. Armodafinil (NAP), modafinil (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of data on foetal outcomes including congenital anomalies from a single observational study in the US

Action: For adoption of PRAC recommendation

EPITT 19367 – Follow-up to February 2019

4.3.2. Direct-acting oral anticoagulants (DOACs): apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/SDA/033; dabigatran etexilate – PRADAXA (CAP) - EMEA/H/C/000829/SDA/049; edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/SDA/011, ROTEAS (CAP); rivaroxaban – XARELTO (CAP) - EMEA/H/C/000944/SDA/047

Applicant(s): Bayer AG (Xarelto), Boehringer Ingelheim (Pradaxa), Bristol-Myers Squibb Pharma EEIG (Eliquis), Daiichi Sankyo Europe (Lixiana, Roteas)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of recurrent thrombosis in patients with antiphospholipid syndrome

Action: For adoption of PRAC recommendation

EPITT 19320 – Follow-up to November 2018

4.3.3. Idelalisib – ZYDELIG (CAP) - EMEA/H/C/003843/SDA/017

Applicant(s): Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

Scope: Signal of arthritis and arthralgia

Action: For adoption of PRAC recommendation

EPITT 19312 – Follow-up to December 2018

4.3.4. Inactivated poliomyelitis vaccine[4] (NAP)

Applicant(s): various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of case reports from outside the EU of immune thrombocytopenic purpura

Action: For adoption of PRAC recommendation

EPITT 19336 – Follow-up to December 2018

4.3.5. Ivacaftor – KALYDECO (CAP) - EMEA/H/C/002494/SDA/025; ivafactor, tezacaftor – SYMKEVI (CAP) - EMEA/H/C/004682/SDA/004

Applicant(s): Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Signal of increased blood creatine phosphokinase (CPK)

Action: For adoption of PRAC recommendation

EPITT 19316 – Follow-up to December 2018

4.3.6. Selective serotonin reuptake inhibitors (SSRI): citalopram (NAP); escitalopram (NAP)

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of drug interaction with fluconazole

Action: For adoption of PRAC recommendation

EPITT 19327 – Follow-up to December 2018

4.3.7. Sorafenib – NEXAVAR (CAP) - EMEA/H/C/000690/SDA/039

Applicant(s): Bayer AG

PRAC Rapporteur: Annika Folin

Scope: Signal of acute generalised exanthematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 18109 – Follow-up to December 2018

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Dolutegravir, lamivudine - EMEA/H/C/004909

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

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

[4] Including combination vaccines

5.1.2. Enasidenib - EMEA/H/C/004324, Orphan

Applicant: Celgene Europe BV

Scope: Treatment of acute myeloid leukaemia (AML)

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

5.1.3. Fluticasone furoate, umeclidinium, vilanterol - EMEA/H/C/005254

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

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

5.1.4. Glucagon - EMEA/H/C/003848

Scope: Treatment of severe hypoglycaemia

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

5.1.5. Polatuzumab vedotin - EMEA/H/C/004870, Orphan

Applicant: Roche Registration GmbH

Scope (accelerated assessment): Treatment of mature B cell lymphomas

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

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

Applicant: Karyopharm Europe GmbH

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

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

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

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

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

5.1.8. Tagraxofusp - EMEA/H/C/005031, Orphan

Applicant: TMC Pharma (EU) Limited

Scope (accelerated assessment): Treatment of adult patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN)

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/WS1521/0105; abacavir, lamivudine - KIVEXA (CAP) - EMEA/H/C/000581/WS1521/0079;

abacavir, lamivudine, zidovudine - TRIZIVIR (CAP) - EMEA/H/C/000338/WS1521/0112

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of a RMP (version 1.0) combining the RMPs for Ziagen (abacavir), Kivexa (abacavir/lamivudine) and Trizivir (abacavir/lamivudine/zidovudine) into one RMP specific to abacavir-active substance and revision of the important identified/potential risk for abacavir-containing products in line with revision 2 of GVP module V on 'Risk management systems', based on the post-marketing data

Action: For adoption of PRAC Assessment Report

5.2.2. Cangrelor - KENGREXAL (CAP) - EMEA/H/C/003773/II/0015

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Update of the RMP (version 2.0) in order to update the requirements for a planned study (listed as a category 3 in the RMP): a multicentre, observational, non-interventional European study of patients undergoing percutaneous coronary intervention (PCI) who receive cangrelor and transition to either clopidogrel, prasugrel or ticagrelor. In addition, the MAH took the opportunity to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.3. Carfilzomib - KYPROLIS (CAP) - EMEA/H/C/003790/II/0034, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of the RMP (version 10) in line with revision 2 of GVP module V on 'Risk management systems', resulting in the reclassification and removal of a number of identified and potential risks and missing information

Action: For adoption of PRAC Assessment Report

5.2.4. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0078/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of an update of the RMP (version 25) in order to: 1) bring it in line with revision 2 of GVP module V on 'Risk management systems'; 2) add study 20170534 (listed as category 3 study in the RMP): an open-label extension of the currently ongoing study 20130173 involving paediatric subjects with osteogenesis imperfecta, based on the MAH's commitment arising from Prolia (denosumab) approved paediatric investigation plan (PIP: EMEA-000145-PIP02-12): open-label, prospective, extension study; 3) add a study (listed as category 3 study in the RMP) to further characterize potential increased risk of cerebrovascular events (stroke) and other serious cardiovascular events in subjects with

osteoporosis, as per the conclusion of periodic safety update single assessment (PSUSA) procedure PSUSA/00000954/201709 adopted in April 2018

Action: For adoption of PRAC Assessment Report

5.2.5. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0081

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 26) in order to amend the study population to men and women who receive denosumab with glucocorticoid exposure and related study objectives for study 20090522 (listed as a category 3 study in the RMP): denosumab global safety assessment among women with postmenopausal osteoporosis and men with osteoporosis in multiple observational databases. The amended protocol for study 20090522 is provided accordingly

Action: For adoption of PRAC Assessment Report

5.2.6. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/II/0039

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 9.0) to replace the current registries with one company-sponsored initiated registry, PERFUSE: one-year persistence to treatment of patients receiving Flixabi (infliximab): a French cohort study; together with three inflammatory bowel disease (IBD) registries, namely: long-term observation registry in German IBD patients (CEDUR), Czech registry of IBD patients on biological therapy (CREDIT) and Dutch network of hospitals IBD registry (DREAM)

Action: For adoption of PRAC Assessment Report

5.2.7. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0062

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of the RMP (version 13.5) in order to introduce a patient information brochure (PIB) as an additional risk minimisation measure (aRMM). Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.8. Pramipexole - MIRAPEXIN (CAP) - EMEA/H/C/000134/WS1510/0089; SIFROL (CAP) - EMEA/H/C/000133/WS1510/0080

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of the RMP (version 9) to implement changes requested in the conclusions of periodic safety update single assessment (PSUSA) PSUSA/00002491/201604 procedure and

in connection with a PRAC signal assessment procedure. In addition, the RMP is updated in order to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template). Furthermore, the MAH took the opportunity to adapt the medical search strategies and data retrieval approach without any impact on the overall safety conclusion

Action: For adoption of PRAC Assessment Report

5.2.9. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/II/0006

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Update of the RMP (version 3.0) in order to reflect that the first milestones (i.e. final protocol submissions) are fulfilled for study NN9535-4447: a cohort study based on Nordic registry data to assess the risk of pancreatic cancer associated with the use of Ozempic (semaglutide) in patients with type 2 diabetes mellitus (T2DM) and study NN9535-4352: a randomised, double-masked parallel-group, placebo-controlled trial assessing the long-term effects of Ozempic (semaglutide) on diabetic retinopathy in subjects with T2DM. In addition, the RMP is updated 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)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0022

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to add two dosing regimens: 840 mg every 2 weeks and 1680 mg every 4 weeks administered as an intravenous (IV) infusion for the approved indications, based on results of population pharmacokinetics modelling and simulation analyses (report No. 1085557) and supported by exposure-response analyses (report No. 1087176). The package leaflet is updated accordingly. In addition, the RMP is updated (version 4.2) in order to reflect the proposed new dosing regimens and in order to align the indication statement for metastatic urothelial carcinoma with the SmPC. Moreover, the due date for submission of RMP commitments and an Annex II condition are proposed to be updated

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

5.3.2. Bevacizumab - AVASTIN (CAP) - EMEA/H/C/000582/II/0106/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped variations consisting of: 1) update of section 5.1 of the SmPC to reflect final overall survival data from the long-term follow-up study JO25567 (erlotinib alone or with bevacizumab as first-line therapy in patients with advanced non-squamous non-small-cell lung cancer (NSCLC) harbouring epidermal growth factor receptor (EGFR) mutations: an open-label, randomised, multicentre, phase 2 study) in order to fulfil ANX 085 for study

JO29424 (survival follow up of JO25567); 2) change in the deadline for the fulfilment of ANX 086 (discussion on any further outcome data on the combination of bevacizumab and erlotinib in the first-line treatment of patients with non-squamous NSCLC harbouring EGFR activating mutations) from Q4 2018 to Q2 2019. Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 29.0) are updated accordingly. The RMP is submitted in line with revision 2 of the guidance on the format of RMP in the EU (template) and consolidates the approved versions (versions 27.1 and 28.1)

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

5.3.3. Ciclosporin - IKERVIS (CAP) - EMEA/H/C/002066/WS1490/0014; VERKAZIA (CAP) - EMEA/H/C/004411/WS1490/0001

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Update of the RMP (version 7.0) in order to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template). The milestones for the Verkazia (ciclosporin) PASS on: quantification of the risk of periocular skin cancer, conjunctival or corneal neoplasia in children treated with Verkazia (ciclosporin) for vernal keratoconjunctivitis (VKC), have also been updated. In addition, the MAH proposed to align Ikervis (ciclosporin) SmPC section 4.4 on concomitant therapy and effects on immune system with Verkazia (ciclosporin) SmPC in order to harmonise the routine risk minimisation measures for both medicinal products. The MAH took this opportunity to implement the latest quality review of documents (QRD) template and the safety features for Ikervis (ciclosporin)

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

5.3.4. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS1539/0029; FORXIGA (CAP) - EMEA/H/C/002322/WS1539/0048; dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/WS1539/0035; XIGDUO (CAP) - EMEA/H/C/002672/WS1539/0046

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Worksharing variations consisting of an update of sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC of Forxiga (dapagliflozin), Edistride (dapagliflozin), Xigduo (dapagliflozin/metformin) and Ebymect (dapagliflozin/metformin) in order to modify the current indication for improvement of glycaemic control based on final results from study D1693C00001 (DECLARE) (listed as a category 3 study in the RMP): 'dapagliflozin effect on cardiovascular events a multicentre, randomized, double-blind, placebo-controlled trial to evaluate the effect of dapagliflozin 10 mg once daily on the incidence of cardiovascular death, myocardial infarction or ischemic stroke in patients with type 2 diabetes' for the prevention of new or worsening heart failure (HF) or cardiovascular (CV) death and for the prevention of new or worsening nephropathy. The package leaflets are updated accordingly. The RMPs for Edistride and Forxiga (version 17) and Ebymect and Xigduo (version 11) are updated accordingly. In addition, the MAH took the opportunity to update the warning on lactose in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'. The MAH also took the opportunity to introduce minor editorial changes in the product information

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

5.3.5. Duloxetine - CYMBALTA (CAP) - EMEA/H/C/000572/WS1527/0078/G; DULOXETINE LILLY (CAP) - EMEA/H/C/004000/WS1527/0014/G; XERISTAR (CAP) - EMEA/H/C/000573/WS1527/0081/G; YENTREVE (CAP) - EMEA/H/C/000545/WS1527/0063/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 4.6 of the SmPC in order to add a warning on the risk of postpartum haemorrhage based on the final results from study F1J-MC-B057 (listed as a category 3 study in the RMP): an observational study to assess maternal and foetal outcomes following exposure to duloxetine. The package leaflet is updated accordingly; 2) enrolment termination for study F1J-MC-B034 (study B034): pregnancy registry to compare the pregnancy and birth outcomes of women given duloxetine during pregnancy with those of an unexposed group of pregnant women. The RMP (version 13) is updated accordingly. In addition, the MAH took the opportunity to correct the term 'sucrase-isomaltase' in section 4.4 of the SmPC 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' and to bring the product information (PI) in line with the latest quality review of documents (QRD) template (version 10). Finally, the MAH proposed to combine into a single SmPC the Xeristar 30 mg SmPC, Xeristar 60 mg SmPC and the Yentreve 20 mg SmPC and Yentreve 40 mg SmPC respectively, following the policy on combined SmPCs (EMA/333423/2015)

See also 10.1.1.

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

5.3.6. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0105, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody (Ab) positive. As a consequence the SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, Annex II are updated. The package leaflet and the RMP (version 19) are updated accordingly

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

5.3.7. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/II/0015

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 4.5 of the SmPC in order to remove the statement on potential drug interactions with drugs that inhibit organic cation transporter 1 (OCT1) based on the final results from study V8953M-SPD503: a non-clinical study on transporter interaction - OCT1 inhibition. The RMP (version 3.0) is updated accordingly

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

5.3.8. Human normal immunoglobulin - FLEBOGAMMA DIF (CAP) - EMEA/H/C/000781/II/0059/G

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) update of section 4.8 of the SmPC for Flebogamma DIF (human normal immunoglobulin) 100 mg/mL in order to update the safety information based on the final results from study IG0601: A multicentre, prospective, open-label, clinical trial to assess the safety and the efficacy of a new intravenous immune globulin (IGIV3I Grifols 10%) in patients with idiopathic (immune) thrombocytopenic purpura. The package leaflet is updated accordingly; 2) update of section 4.8 of the SmPC to revise the adverse drug reactions for both strengths based on all completed studies previously submitted. The package leaflet is updated accordingly; 3) update of SmPC according to the Guideline on core SmPC for human normal immunoglobulin for intravenous administration (IVIg) which came into effect on 01 January 2019.The package leaflet and the RMP (version 7.0) are updated accordingly

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

5.3.9. Insulin aspart - FIASP (CAP) - EMEA/H/C/004046/II/0010

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of children and adolescents aged 1 year and above based on data from study NN1218-4101: a phase 3b study on efficacy and safety of faster-acting insulin aspart compared to Novorapid (insuplin aspart) both in combination with insulin degludec in children and adolescents with type 1 diabetes; supported by data from study NN1218-4371: a trial comparing the pharmacokinetic properties of fast-acting insulin aspart between children, adolescents and adults with type 1 diabetes; and study NN1218-3888: a trial investigating the pharmacokinetic properties of Fiasp (insulin aspart) in children, adolescents and adults with type 1 diabetes. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC and the corresponding sections of the package leaflet are updated accordingly. In addition, the MAH took the opportunity to introduce other non-related minor or editorial changes throughout the product information to increase readability/consistency

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

5.3.10. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/X/0169

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

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

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

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

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

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

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

5.3.12. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/X/0075/G, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped applications consisting of: 1) extension application to add a new strength of 25 mg granules in sachet in the treatment of cystic fibrosis in children aged 6 to less than 12 months old; 2) update of sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC, and sections 2 and 3 of the package leaflet for the 150 mg film-coated tablet presentation to bring it in line with the new dosage form (25 mg granules). The RMP (version 8.3) is updated accordingly. In addition, the MAH took the opportunity to implement minor updates in the product information

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

5.3.13. Lacosamide - VIMPAT (CAP) - EMEA/H/C/000863/II/0073/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.4, 4.5 and 4.8 of the SmPC in order to include new safety information on cardiac arrhythmias based on safety signal assessment report (SSAR); 2) update of section 4.8 of the SmPC to update the frequency of some adverse events (AEs) based on data obtained from the updated safety pool analysis (Pool DBC-1) which consists of the combined data from SP667, SP754, SP755, and EP0008. All of these studies were randomized, double-blind, placebo-controlled, parallel-group, adjunctive therapy studies in subjects with epilepsy. The package leaflet and the RMP (version 13.0) are updated accordingly

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

5.3.14. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0069

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include first line treatment of advanced or metastatic renal cell carcinoma (RCC) as combination therapy of pembrolizumab together with axitinib based on the results of the first interim analysis (IA1) from pivotal study KN426: an ongoing, phase 3, randomized, open-label, multicentre, global study to evaluate the efficacy and safety of pembrolizumab in combination with axitinib versus sunitinib in previously untreated subjects with advanced/metastatic RCC. It also includes supportive data from KEYNOTE-427 Cohort A (pembrolizumab monotherapy): pembrolizumab monotherapy as first-line therapy in advanced clear cell RCC (ccRCC) and sponsored study A4061051 (axitinib monotherapy): axitinib for the treatment of metastatic RCC. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 24.1) 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

5.3.15. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[5]) - EMEA/H/W/002300/II/0036

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.4 of the SmPC in order to modify the warning on 'protection against *Plasmodium falciparum* malaria' over time. This update is based on the final results from study MALARIA-076 (listed as a category 3 study in the RMP): an open extension to phase 3, multicentre study MALARIA-055 PRI (110021) to evaluate long-term efficacy, safety and immunogenicity of Mosquirix (plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted)) malaria vaccine in infants and children. The RMP (version 4.1) is updated accordingly

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

5.3.16. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/II/0022

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Update of Sections 4.2, 4.4 and 4.5 of the SmPC in order to update the safety information based on the final results from study AC-065-117 (listed as a category 3 study in the RMP): clinical pharmacology drug-drug interaction (DDI) study evaluating the effect of clopidogrel a moderate inhibitor of CYP2C8[6], on the pharmacokinetics of selexipag and its active metabolite ACT-333679. The package leaflet and the RMP (version 6.1) are updated accordingly. In addition, the MAH took the opportunity to correct minor discrepancies in the SmPC

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

5.3.17. Smallpox vaccine (live modified vaccinia virus Ankara) - IMVANEX (CAP) - EMEA/H/C/002596/II/0036

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information and to provide confirmation in terms of immunogenicity based on the results from study POX-MVA-006 (listed as an obligation in Annex II (ANX 004)): a randomized, open-label phase 3 non-inferiority trial to compare indicators of efficacy for smallpox vaccine to the US licensed replicating smallpox vaccine in 18-42 year old healthy vaccinia-naïve subjects. The package leaflet and the RMP (version 7.2) are updated accordingly

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

[5] Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)
[6] Cytochrome P450 2C8

5.3.18. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS1518/0055; sofosbuvir, ledipasvir - HARVONI (CAP) - EMEA/H/C/003850/WS1518/0077; sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/WS1518/0034; sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/WS1518/0025

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Worksharing variation to update sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Epclusa (sofosbuvir/velpatasvir) and Harvoni (sofosbuvir/ledipasvir), sections 4.2, 4.4, 5.1 and 5.2 for Sovaldi (sofosbuvir) and sections 4.2, 4.8 and 5.2 for Vosevi (sofosbuvir/velpatasvir/voxilaprevir) in order to add new information regarding the use of sofosbuvir-containing products in patients with renal impairment, based on the final results from studies: 1) GS-US-342-4062 (listed as a category 3 study in the RMP): a phase 2, multicentre, open-label study to evaluate the efficacy and safety of sofosbuvir/velpatasvir for 12 weeks in subjects with chronic hepatitis C virus (HCV) infection who are on dialysis for end stage renal disease; 2) GS-US-337-4063 (listed as a category 3 study in the RMP): a phase 2, multicentre, open-label study to evaluate the efficacy and safety of ledipasvir/sofosbuvir in subjects with genotype 1, 4, 5 and 6 chronic HCV infection who are on dialysis for end stage renal disease; 3) GS-US-334-0154 (listed as a category 3 study in the RMP): a phase 2b, open label study of 200 mg or 400 mg Sofosbuvir+ribavirin for 24 weeks in genotype 1 or 3 HCV infected subjects with renal insufficiency; 4) study GS-US-338-1125: a phase 1, open-label, parallel-group, single-dose study to evaluate the pharmacokinetics of voxilaprevir in subjects with normal renal function and severe renal impairment. The package leaflet is updated accordingly. The RMPs for Epclusa (version 4.1), Harvoni (version 5.1), Sovaldi (version 8.1) and Vosevi (version 2.1) are updated accordingly

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

5.3.19. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0071

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication for Stelara to include treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies. As a consequence, the SmPC, package leaflet and RMP (version 15.0) are updated

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. Aliskiren - RASILEZ (CAP); aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - PSUSA/00000089/201809

Applicant: Noden Pharma DAC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alemtuzumab - LEMTRADA (CAP) - PSUSA/00010055/201809 (with RMP)

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Avelumab - BAVENCIO (CAP) - PSUSA/00010635/201809

Applicant: Merck Europe B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Ciclosporin[7] - IKERVIS (CAP); VERKAZIA (CAP) - PSUSA/00010362/201809

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Daptomycin - CUBICIN (CAP) - PSUSA/00000931/201809

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[7] Topical use only

6.1.6. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA (CAP) - PSUSA/00010646/201809

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Darvadstrocel - ALOFISEL (CAP) - PSUSA/00010676/201809

Applicant: Takeda Pharma A/S, ATMP[8]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.8. Denosumab[9] - PROLIA (CAP) - PSUSA/00000954/201809

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Denosumab[10] - XGEVA (CAP) - PSUSA/00009119/201809

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Dexamethasone[11] - NEOFORDEX (CAP) - PSUSA/00010480/201809

Applicant: Laboratoires CTRS

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Dulaglutide - TRULICITY (CAP) - PSUSA/00010311/201809

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

[8] Advanced therapy medicinal product
[9] Indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer only
[10] Indicated for skeletal related events associated with bone metastases and for giant cell tumour of bone only
[11] Centrally authorised product indicated in symptomatic multiple myeloma only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Dupilumab - DUPIXENT (CAP) - PSUSA/00010645/201809

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Eftrenonacog alfa - ALPROLIX (CAP) - PSUSA/00010499/201809

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Eltrombopag - REVOLADE (CAP) - PSUSA/00001205/201809

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Eluxadoline - TRUBERZI (CAP) - PSUSA/00010528/201809

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Etravirine - INTELENCE (CAP) - PSUSA/00001335/201809

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Ferric citrate coordination complex - FEXERIC (CAP) - PSUSA/00010418/201809

Applicant: Keryx Biopharma UK Ltd.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Fluticasone furoate, umeclidinium, vilanterol - ELEBRATO ELLIPTA (CAP); TRELEGY ELLIPTA (CAP) - PSUSA/00010653/201809

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Glycopyrronium[12] - SIALANAR (CAP) - PSUSA/00010529/201809

Applicant: Proveca Pharma Limited

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Human coagulation factor X - COAGADEX (CAP) - PSUSA/00010481/201809

Applicant: BPL Bioproducts Laboratory GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Idebenone[13] - RAXONE (CAP) - PSUSA/00010412/201809

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Insulin aspart - FIASP (CAP); NOVOMIX (CAP); NOVORAPID (CAP) - PSUSA/00001749/201809

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Insulin degludec, liraglutide - XULTOPHY (CAP) - PSUSA/00010272/201809

Applicant: Novo Nordisk A/S

[12] Centrally authorised product indicated for the treatment of severe siallorhea only
[13] Centrally authorised product(s) only

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Isavuconazole - CRESEMBA (CAP) - PSUSA/00010426/201809 (with RMP)

Applicant: Basilea Pharmaceutica Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Ixekizumab - TALTZ (CAP) - PSUSA/00010493/201809

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Lacosamide - VIMPAT (CAP) - PSUSA/00001816/201808

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Mepolizumab - NUCALA (CAP) - PSUSA/00010456/201809

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Moroctocog alfa - REFACTO AF (CAP) - PSUSA/00002089/201808

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Naloxegol - MOVENTIG (CAP) - PSUSA/00010317/201809

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Naltrexone, bupropion - MYSIMBA (CAP) - PSUSA/00010366/201809

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Niraparib - ZEJULA (CAP) - PSUSA/00010655/201809

Applicant: Tesaro Bio Netherlands B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Ocrelizumab - OCREVUS (CAP) - PSUSA/00010662/201809

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Oritavancin - ORBACTIV (CAP) - PSUSA/00010368/201809

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Panitumumab - VECTIBIX (CAP) - PSUSA/00002283/201809

Applicant: Amgen Europe B.V.

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Pitolisant - WAKIX (CAP) - PSUSA/00010490/201809

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Raltegravir - ISENTRESS (CAP) - PSUSA/00010373/201809

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Ribociclib - KISQALI (CAP) - PSUSA/00010633/201809

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Riociguat - ADEMPAS (CAP) - PSUSA/00010174/201809

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Rivaroxaban - XARELTO (CAP) - PSUSA/00002653/201809

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Rucaparib - RUBRACA (CAP) - PSUSA/00010694/201809

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Sodium zirconium cyclosilicate - LOKELMA (CAP) - PSUSA/00010675/201809

Applicant: AstraZeneca AB

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Tildrakizumab - ILUMETRI (CAP) - PSUSA/00010720/201809

Applicant: Almirall S.A

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Tobramycin[14] - VANTOBRA[15] - PSUSA/00010370/201809 (with RMP)

Applicant: PARI Pharma GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Trabectedin - YONDELIS (CAP) - PSUSA/00003001/201809

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Trientine - CUPRIOR (CAP) - PSUSA/00010637/201809

Applicant: GMP-Orphan SA

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Velmanase alfa - LAMZEDE (CAP) - PSUSA/00010677/201809

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Vortioxetine - BRINTELLIX (CAP) - PSUSA/00010052/201809

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

[14] Nebuliser solution, centrally authorised product(s) only
[15] European Commission (EC) decision on the MA withdrawal of Vantobra dated 18 February 2019

Action: For adoption of recommendation to CHMP

6.1.48. Zoledronic acid[16] - ACLASTA (CAP) - PSUSA/00009334/201808

Applicant: Novartis Europharm Limited

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. Anagrelide - ANAGRELIDE MYLAN (CAP); XAGRID (CAP); NAP - PSUSA/00000208/201809

Applicant(s): Mylan S.A.S (Anagrelide Mylan), Shire Pharmaceuticals Ireland Limited (Xagrid), various

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Zoledronic acid[17] - ZOLEDRONIC ACID HOSPIRA (CAP); ZOLEDRONIC ACID MEDAC (CAP); ZOMETA (CAP); NAP - PSUSA/00003149/201808

Applicant(s): Medac Gesellschaft fur klinische Spezialpraparate mbH (Zoledronic acid medac), Novartis Europharm Limited (Zometa), Pfizer Europe MA EEIG (Zoledronic acid Hospira), various

PRAC Rapporteur: Anette Kirstine Stark

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. Aztreonam[18] (NAP) - PSUSA/00010178/201808

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[16] Indicated for osteoporosis only
[17] Indicated for cancer and fractures only
[18] Parenteral use only

6.3.2. Chloroquine (NAP) - PSUSA/00000685/201808

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Ciclesonide (NAP) - PSUSA/00000742/201808

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Dexamfetamine (NAP) - PSUSA/00000986/201809

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Finasteride (NAP) - PSUSA/00001392/201808

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Fluocinolone acetonide[19] (NAP) - PSUSA/00010224/201808

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Rilmenidine (NAP) - PSUSA/00002643/201808

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[19] Intravitreal implant in applicator only

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/LEG 034

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Detailed review of cases of alopecia in patients using apixaban from post marketing cases, clinical trial data, and literature including cases with a possible or probable relationship due to missing information, as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00000226/201805 adopted at the December 2018 PRAC meeting (held on 26-29 November 2018)

Action: For adoption of advice to CHMP

6.4.2. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/LEG 035

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Detailed review of cases of worsening of renal function in patients using apixaban from post marketing cases, clinical trial data, and literature including cases with a possible or probable relationship due to missing information, as requested in the conclusions of the periodic safety update single assessment procedure PSUSA/00000226/201805 adopted at the December 2018 PRAC meeting (held on 26-29 November 2018)

Action: For adoption of advice to CHMP

6.4.3. Clopidogrel - CLOPIDOGREL ZENTIVA (CAP) - EMEA/H/C/000975/LEG 014

Applicant: Zentiva k.s.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Review of the risk of interaction between morphine and clopidogrel as agent of the class of $P2Y_{12}$ inhibitors, as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00002499/201802 for prasugrel adopted in September 2018

Action: For adoption of advice to CHMP

6.4.4. Clopidogrel - ISCOVER (CAP) - EMEA/H/C/000175/LEG 032

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Review of the risk of interaction between morphine and clopidogrel as agent of the class of $P2Y_{12}$ inhibitors, as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00002499/201802 for prasugrel adopted in September 2018

Action: For adoption of advice to CHMP

6.4.5. Clopidogrel - PLAVIX (CAP) - EMEA/H/C/000174/LEG 035

Applicant: Sanofi Clir SNC

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Review of the risk of interaction between morphine and clopidogrel as agent of the class of $P2Y_{12}$ inhibitors, as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00002499/201802 for prasugrel adopted in September 2018

Action: For adoption of advice to CHMP

6.4.6. Clopidogrel, acetylsalicylic acid - CLOPIDOGREL/ACETYLSALICYLIC ACID ZENTIVA (CAP) - EMEA/H/C/001144/LEG 010

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Review of the risk of interaction between morphine and clopidogrel as agent of the class of $P2Y_{12}$ inhibitors, as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00002499/201802 for prasugrel adopted in September 2018

Action: For adoption of advice to CHMP

6.4.7. Clopidogrel, acetylsalicylic acid - DUOPLAVIN (CAP) - EMEA/H/C/001143/LEG 013

Applicant: Sanofi Clir SNC

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Review of the risk of interaction between morphine and clopidogrel as agent of the class of $P2Y_{12}$ inhibitors, as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00002499/201802 for prasugrel adopted in September 2018

Action: For adoption of advice to CHMP

6.4.8. Interferon beta-1a - REBIF (CAP) - EMEA/H/C/000136/LEG 044

Applicant: Merck Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Detailed justification regarding the decrease of spontaneous reports during the period covered by the PSUSA procedure together with a cumulative review of cases of panniculitis, as requested in the conclusions of periodic single assessment procedure PSUSA/00009198/201805 adopted at the December 2018 PRAC (held on 26-29 November 2018)

Action: For adoption of advice to CHMP

6.4.9. Pixantrone - PIXUVRI (CAP) - EMEA/H/C/002055/LEG 012

Applicant: CTI Life Sciences Deutschland GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Detailed review for all phase 3 trials including study PIX306[20] as well as for study

[20] A randomised multicentre study comparing pixantrone + rituximab with gemcitabine + rituximab in patients with aggressive B-cell non-Hodgkin lymphoma who have relapsed after therapy with CHOP-R (cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisone - rituximab) or an equivalent regimen and are ineligible for stem cell transplant

PIXreal[21] of the number and proportion of patients for each study with information on possible dose lowering and/or dose omission/skipping, as requested in the conclusions of periodic single assessment procedure PSUSA/00009261/201805 adopted at the December 2018 PRAC (held on 26-29 November 2018)

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[22]

7.1.1. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/PSP/S/0066.1

Applicant: Novartis Europharm Ltd, ATMP[23]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to PSA/S/0031 [protocol for non-interventional study CCTL019B2401 with secondary use of data from two registries conducted by the 'European Society for Blood and Marrow Transplantation' (EBMT) and 'Centre for International Blood and Marrow Transplant Research' (CIBMTR) to evaluate the long term safety of patients with B lymphocyte malignancies treated with tisagenlecleucel (chimeric antigen receptor (CAR)-T cell therapy) in a real-world setting] as per the request for supplementary information (RSI) adopted in December 2018

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

7.1.2. Tolvaptan - JINARC (CAP) - EMEA/H/C/PSA/S/0031.1

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to PSA/S/0031 [amendment to a protocol initially endorsed by PRAC in March 2016 (PSP/0028.2) for a 4-year, multicentre, non-interventional PASS to measure the effectiveness of the risk minimisation measures in reducing the severity of liver injury in patients who experience an elevation of transaminase (alanine aminotransferase [ALT] or aspartate aminotransferase [AST]) > 3× upper limit of normal (ULN), or an adverse event (AE) consistent with hepatotoxicity in real life] as per the request for supplementary information (RSI) adopted in October 2018

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

7.1.3. Voretigene neparvovec - LUXTURNA (CAP) - EMEA/H/C/PSP/S/0078

Applicant: Novartis Europharm Ltd, ATMP[24]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for a post-authorisation observational study to collect long-term safety

[21] An observational, multicentre, open label study of pixantrone 50mg/m² given on days 1, 8, and 15 of each 28 day cycle for up to 6 cycles for the treatment of adult patients with multiple relapsed or refractory aggressive B cell non-Hodgkin lymphomas
[22] In accordance with Article 107n of Directive 2001/83/EC
[23] Advanced therapy medicinal product
[24] Advanced therapy medicinal product

information (i.e., for 5 years after treatment) associated with voretigene neparvovec (vector and/or transgene), its subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[25]

7.2.1. Adalimumab - AMGEVITA (CAP) - EMEA/H/C/004212/MEA 001

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study 20160264 (ABP 501) - British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR): an observational study to evaluate long term safety of Amgevita (adalimumab) in patients with rheumatoid arthritis [final report due date: Q3 2027] (from initial MA/opinion)

Action: For adoption of advice to CHMP

7.2.2. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 009.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 009 [PASS protocol for study I4V-MC-B0166: assessment of off-label use in paediatric patients in the UK in the Clinical Practice Research Datalink (CPRD) database] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

7.2.3. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/MEA 003.4

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 003.3 [protocol for study ML39302 (COVENIS) (listed as a category 3 study in the RMP): a non-interventional study to investigate the effectiveness, safety and utilisation of cobimetinib and vemurafenib in patients with and without brain metastases with BRAF V600 mutant melanoma under real world conditions (final clinical study report (CSR) due date: December 2022)] as per the request for supplementary information (RSI) adopted in November 2018

Action: For adoption of advice to CHMP

7.2.4. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 002.7

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002.6 [amendment to previously agreed protocol for study

[25] 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

1245.96 (version 5.0): an observational cohort study using existing data including urinary tract infection (UTI) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors] as per the request for supplementary information (RSI) adopted in October 2018

Action: For adoption of advice to CHMP

7.2.5. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/MEA 004.3

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 004.2 [amendment to previously agreed protocol for study 1245.96 (version 5.0): an observational cohort study using existing data including urinary tract infection (UTI) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors] as per the request for supplementary information (RSI) adopted in October 2018

Action: For adoption of advice to CHMP

7.2.6. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 003.4

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 003.3 [amendment to previously agreed protocol for study 1245.96 (version 5.0): an observational cohort study using existing data including urinary tract infection (UTI) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors] as per the request for supplementary information (RSI) adopted in October 2018

Action: For adoption of advice to CHMP

7.2.7. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003

Applicant: Almirall S.A

PRAC Rapporteur: Adrien Inoubli

Scope: Protocol for study M-14745-40: European Psoriasis Registry to collect long-term safety data for tildrakizumab and to further characterise the long-term safety profile of tildrakizumab in the treatment of psoriasis under conditions of routine clinical (from initial MAA/opinion)

Action: For adoption of advice to CHMP

7.2.8. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 045.3

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA-045.2 [protocol for study RRA-20745: a PASS to investigate

the long-term safety in adult patients with moderately to severely active Crohn's disease] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[26]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[27]

7.4.1. Adalimumab - HULIO (CAP) - EMEA/H/C/004429/II/0004

Applicant: Mylan S.A.S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study FKB327-003 (listed as a category 3 study in the RMP): an open-label extension study to compare the long term efficacy, safety, immunogenicity and pharmacokinetics of Hulio (adalimumab) and Humira (adalimumab) in patients with rheumatoid arthritis on concomitant methotrexate (ARABESC-OLE). The RMP (version 2.0) is updated accordingly. In addition, the MAH took the opportunity to remove the product information text from Annex 6 of the RMP and proposed to only keep the text for patient alert card in the RMP as an additional risk minimisation measure

Action: For adoption of PRAC Assessment Report

7.4.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0185

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from the Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) registry (listed as a category 3 study in the RMP): an ongoing long-term observational cohort study initiated in Germany in 2001 by the German Society of Rheumatology to investigate the long-term safety, effectiveness, and costs of biologic therapies for rheumatoid arthritis

Action: For adoption of PRAC Assessment Report

7.4.3. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0054

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Submission of the final study report, as requested by PRAC in the conclusions of MEA 11.5 adopted at the October 2016 meeting, from study H80-MC-B015 extension/D5550R00003: 'incidence of pancreatic malignancy and thyroid neoplasm in type 2 diabetes mellitus (T2DM) patients who initiate exenatide compared to other antihyperglycemic drugs' as well as the feasibility study on 'incidence of pancreatic cancer and thyroid neoplasm among T2DM who initiated Bydureon (exenatide) as compared with those who initiated other

[26] In accordance with Article 107p-q of Directive 2001/83/EC
[27] 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

glucose lowering drugs'. The RMP (version 33) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP) - EMEA/H/C/002673/WS1568/0043; REVINTY ELLIPTA (CAP) - EMEA/H/C/002745/WS1568/0041

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study HZC102972 (listed as a category 3 study in the RMP): a PASS to further characterise the important potential risk of decreased bone mineral density (BMD) and associated fractures with fluticasone furoate (FF)/vilanterol (VI) in the treatment of chronic obstructive pulmonary disease (COPD) by evaluating the effect of the inhaled corticosteroid fluticasone furoate (FF) on bone mineral density by comparing FF/VI treatment with VI treatment in subjects with moderate COPD

Action: For adoption of PRAC Assessment Report

7.4.5. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0085

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study CNTO148ART4002 (listed as a category 3 study in the RMP): an observational phase 4 study using the Optum Research Database (ORD) to estimate the long-term safety profile in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) who are initiating Simponi (golimumab) treatment and/or other types of biologic and non-biologic treatments. The RMP (version 19.0) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems' in order to reflect changes in the categorisation of safety concerns

Action: For adoption of PRAC Assessment Report

7.4.6. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0218

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final study report from the Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) cohort 2 portion of the registry: a German rheumatoid arthritis (RA) registry established as a prospective observational cohort study on the long-term safety and effectiveness of biologic disease-modifying anti-rheumatic drugs (DMARDs) in patients with RA. The RMP (version 19) is updated accordingly. The MAH also revised the RMP list of safety concerns as requested in the conclusions of procedure LEG 156 adopted in October 2017

Action: For adoption of PRAC Assessment Report

7.4.7. Loxapine - ADASUVE (CAP) - EMEA/H/C/002400/II/0030

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final report from drug utilisation study AMDC-204-403 EU (listed as a category 3 study in the RMP): a multinational retrospective medical record review to evaluate utilisation patterns of Adasuve (loxapine) for inhalation in agitated persons in routine clinical care. The RMP (version 9.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. Teriparatide - MOVYMIA (CAP) - EMEA/H/C/004368/II/0010

Applicant: Stada Arzneimittel AG

PRAC Rapporteur: Ronan Grimes

Scope: Submission of the final clinical study report from study RGB1023O31: a phase 3, multicentre, randomised, active-controlled, parallel-group, comparative study to evaluate the efficacy and safety of Movymia (teriparatide) to the originator medicinal product containing teriparatide in patients with osteoporosis at high risk of fracture. The RMP (version 1.3) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.9. Teriparatide - TERROSA (CAP) - EMEA/H/C/003916/II/0009

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ronan Grimes

Scope: Submission of the final clinical study report from study RGB1023O31: a phase 3, multicentre, randomised, active-controlled, parallel-group, comparative study to evaluate the efficacy and safety of Terrosa (teriparatide) to the originator medicinal product containing teriparatide in patients with osteoporosis at high risk of fracture. The RMP (version 1.3) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.8

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Fourth annual report for study OBS13434: a prospective, multicentre, observational PASS to evaluate the long term safety profile of Lemtrada (alemtuzumab) treatment in patients with relapsing forms of multiple sclerosis (MS) and to determine the incidence of adverse events of special interest (AESIs)

Action: For adoption of advice to CHMP

7.5.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 024.10

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Annual report on adverse events and/or lack of efficacy, immunological data, follow-up growth disturbances in children and data on urinary hexose tetrasaccharide (Hex4) from the Pompe registry: a global, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease. The registry aims at detecting adverse events and/or lack of efficacy in patients, and at collecting immunological data, and follow-up growth disturbances in children

Action: For adoption of advice to CHMP

7.5.3. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 025.10

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Annual report on data on patients with renal or hepatic insufficiency from the Pompe registry: a global, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease. The registry aims at detecting adverse events and/or lack of efficacy in patients, and at collecting immunological data, and follow-up growth disturbances in children

Action: For adoption of advice to CHMP

7.5.4. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/MEA 002.5

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 002.4 [third progress report and first interim report for study H9X-MC-B009: dulaglutide European modified prescription-event monitoring and network database study: a multi-database collaborative research programme of observational studies to monitor the utilisation and safety of dulaglutide in the EU] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

7.5.5. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 005.1

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 005 request for supplementary for information (RSI) adopted in March 2018 and second interim report for an enhanced pharmacovigilance study 1245.146 to evaluate the risk of diabetic ketoacidosis (DKA) in patients treated with empagliflozin-containing product(s) as discussed with the FDA and requested in the conclusions of the referral procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) (EMEA/H/A-20/1419) finalised in 2016 [final clinical study report (CSR): Q4/2021]

Action: For adoption of advice to CHMP

7.5.6. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/MEA 005.1

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 005 request for supplementary for information (RSI) adopted in March 2018 and second interim report for an enhanced pharmacovigilance study 1245.146 to evaluate the risk of diabetic ketoacidosis (DKA) in patients treated with empagliflozin-containing product(s) as discussed with the FDA and requested in the conclusions of the referral procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) (EMEA/H/A-20/1419) finalised in 2016 [final clinical study report (CSR): Q4/2021]

Action: For adoption of advice to CHMP

7.5.7. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 002.1

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002 request for supplementary for information (RSI) adopted in March 2018 and second interim report for an enhanced pharmacovigilance study 1245.146 to evaluate the risk of diabetic ketoacidosis (DKA) in patients treated with empagliflozin-containing product(s) as discussed with the FDA and requested in the conclusions of the referral procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) (EMEA/H/A-20/1419) finalised in 2016 [final clinical study report (CSR): Q4/2021]

Action: For adoption of advice to CHMP

7.5.8. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 002.2

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Third annual interim report from an established nationwide register (British Society for Rheumatology Rheumatoid Arthritis Register (BSRBR-RA)) for patients with rheumatological disorders treated with biologic agents, designed as a national prospective study whose primary purpose is to assess long-term toxicity from the use of these agents in routine practice

Action: For adoption of advice to CHMP

7.5.9. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 003.2

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Third annual interim report from an established nationwide register (Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)) for patients with rheumatological disorders treated with biologic agents, designed as a national prospective study whose primary purpose is to assess long-term toxicity from the use of these agents in routine practice

Action: For adoption of advice to CHMP

7.5.10. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 004.2

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Third annual interim report for study from ARTIS (Anti-Rheumatic Treatment in Sweden) register: a national prospective, observational, uncontrolled cohort study evaluating the risk of selected adverse events (AEs) in rheumatoid arthritis (RA), juvenile idiopathic arthritis, and other rheumatic disease patients treated with etanercept

Action: For adoption of advice to CHMP

7.5.11. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 005.2

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Third annual interim report for study from BADBIR (British Association of Dermatologists Biologic Interventions Register) register: a national prospective, observational, uncontrolled cohort study evaluating the risk of selected adverse events (AEs) in rheumatoid arthritis (RA), juvenile idiopathic arthritis, and other rheumatic disease patients treated with etanercept

Action: For adoption of advice to CHMP

7.5.12. Follitropin alfa - OVALEAP (CAP) - EMEA/H/C/002608/MEA 002.4

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002.3 [interim report for study XM17-WH-50005 (SOFIA): a non-interventional multinational prospective observational study to assess the safety of Ovaleap (follitropin alfa) compared to Gonal-F (follitropin alfa) in one treatment cycle with respect to the incidence rates of ovarian hyperstimulation syndrome (OHSS) in infertile women undergoing superovulation for assisted reproductive technologies (ART)] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

7.5.13. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 033.2

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study MK-8259-050: an observational PASS for golimumab in treatment of poly-articular juvenile idiopathic arthritis (pJIA) using the German Biologics JIA registry (BiKeR)

Action: For adoption of advice to CHMP

7.5.14. Insulin detemir - LEVEMIR (CAP) - EMEA/H/C/000528/MEA 045.10

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Anette Kirstine Stark

Scope: Fifth annual progress report for diabetes pregnancy registry (NN304-4016): an international non-interventional prospective cohort study to evaluate the safety of treatment with insulin detemir in pregnant women with diabetes mellitus] as per the request for supplementary information (RSI) adopted in April 2018

Action: For adoption of advice to CHMP

7.5.15. Lonoctocog alfa - AFSTYLA (CAP) - EMEA/H/C/004075/MEA 002

Applicant: CSL Behring GmbH

PRAC Rapporteur: Daniela Philadelphy

Scope: Progress report for study CSL627_3001: a multicentre, open-label, phase 3 extension study which will investigate the safety and efficacy of recombinant factor VIII (rVIII)-single chain for prophylaxis and on-demand treatment of bleeding episodes in a total of at least 250 subjects with severe congenital haemophilia A

Action: For adoption of advice to CHMP

7.5.16. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/MEA 008.5

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 008.4 [second annual interim report for study CA209234 (listed as a category 3 study in the RMP): a PASS exploring the pattern of use, safety, and effectiveness of nivolumab in routine oncology practice [final clinical study report (CSR) due date: 31 December 2024] (from initial opinion/MA)] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

7.5.17. Octocog alfa - IBLIAS (CAP) - EMEA/H/C/004147/MEA 004

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Ninth annual European Haemophilia Safety Surveillance (EUHASS) report/first report for Iblias (octocog alfa) for study study 14149: evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry

Action: For adoption of advice to CHMP

7.5.18. Octocog alfa - HELIXATE NEXGEN (CAP) - EMEA/H/C/000276/MEA 085.7

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Ninth annual European Haemophilia Safety Surveillance (EUHASS) report for study study 14149: evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry

Action: For adoption of advice to CHMP

7.5.19. Octocog alfa - KOGENATE BAYER (CAP) - EMEA/H/C/000275/MEA 086.7

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Ninth annual European Haemophilia Safety Surveillance (EUHASS) report for study study 14149: evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry

Action: For adoption of advice to CHMP

7.5.20. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 004.1

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Ninth annual European Haemophilia Safety Surveillance (EUHASS) report for study study 14149: evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry

Action: For adoption of advice to CHMP

7.5.21. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/MEA 060

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Sixth monthly summary report of medication error events reported with the on body injector in the EU market (from variation II/093/G)

Action: For adoption of advice to CHMP

7.5.22. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/ANX 003.4

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Second biennial interim results 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

Action: For adoption of advice to CHMP

7.5.23. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.16

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: 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

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 014.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 014 [protocol for meta-analysis of amputation events from clinical trials DIA3008 (CANVAS: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of JNJ-28431754 (canagliflozin) on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus (T2DM)), DIA4003 (CANVAS-R: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on renal endpoints in adult subjects with T2DM), and DNE3001 (CREDENCE: a randomised, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and diabetic nephropathy), as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442)] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 013.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 013 [protocol for meta-analysis of amputation events from clinical trials DIA3008 (CANVAS: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of JNJ-28431754 (canagliflozin) on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus (T2DM)), DIA4003 (CANVAS-R: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on renal endpoints in adult subjects with T2DM), and DNE3001 (CREDENCE: a randomised, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and diabetic nephropathy), as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442)] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

7.6.3. Eribulin - HALAVEN (CAP) - EMEA/H/C/002084/MEA 022

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: Statistical analysis plan for study E7389-M044-504: an observational

post-authorisation, single-arm, prospective, multicentre cohort study to investigate the frequency of and time to resolution of eribulin-induced or aggravated peripheral neuropathy (PN) in patients with locally advanced or metastatic breast cancer in a real-life setting (from variation II/33)

Action: For adoption of advice to CHMP

7.6.4. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 038

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Amendment to the previously agreed protocol for study D2311: a phase 3, double-blind, double dummy, randomized, multicentre, active controlled study evaluating efficacy and safety of fingolimod once daily versus interferon β-1a once weekly in paediatric patients with multiple sclerosis (MS) aged 10 to <18 years old (from X/44/G)

Action: For adoption of advice to CHMP

7.6.5. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/MEA 016

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Pooled analysis of non-interventional registry data from a minimum of 3,100 patients aiming at evaluating the risk of tuberculosis and serious infections (in fulfilment of MEA 016). The analysis includes pooled data from studies: 1) Korean post-marketing surveillance (PMS) observational study; 2) study CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra/Remsima (infliximab) in patients with rheumatoid arthritis (EU); 3) registry CT P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra/Remsima (infliximab) in patients with Crohn's disease (CD) or ulcerative colitis (UC) (EU and Korea); 4) registry CT P13 4.4: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra/Remsima (infliximab) in patients with ankylosing spondylitis (EU); 5) British Society for Rheumatology Biologics Register – Rheumatoid Arthritis (BSRBR-RA): a longitudinal observational study of patients with rheumatoid arthritis treated with biologic and other new advanced targeted therapies (UK); 6) Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT): long-term observation of treatment with biologics in rheumatoid arthritis (Germany); 7) PERSIST: a prospective observational cohort study to assess persistence of Inflectra/Remsima (infliximab) in patients with rheumatoid diseases who are either naive to biologics or switched from stable infliximab originator's containing product; 8) post-marketing observational cohort study of patients with inflammatory bowel disease (IBD) treated with Inflectra/Remsima (infliximab) in usual clinical practice (CONNECT-IBD)

Action: For adoption of advice to CHMP

7.6.6. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 016

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Pooled analysis of non-interventional registry data from a minimum of 3,100 patients

aiming at evaluating the risk of tuberculosis and serious infections (in fulfilment of MEA 016). The analysis includes pooled data from studies: 1) Korean post-marketing surveillance (PMS) observational study; 2) study CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra/Remsima (infliximab) in patients with rheumatoid arthritis (EU); 3) registry CT P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra/Remsima (infliximab) in patients with Crohn's disease (CD) or ulcerative colitis (UC) (EU and Korea); 4) registry CT P13 4.4: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra/Remsima (infliximab) in patients with ankylosing spondylitis (EU); 5) British Society for Rheumatology Biologics Register – Rheumatoid Arthritis (BSRBR-RA): a longitudinal observational study of patients with rheumatoid arthritis treated with biologic and other new advanced targeted therapies (UK); 6) Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT): long-term observation of treatment with biologics in rheumatoid arthritis (Germany); 7) PERSIST: a prospective observational cohort study to assess persistence of Inflectra/Remsima (infliximab) in patients with rheumatoid diseases who are either naive to biologics or switched from stable infliximab originator's containing product; 8) post-marketing observational cohort study of patients with inflammatory bowel disease (IBD) treated with Inflectra/Remsima (infliximab) in usual clinical practice (CONNECT-IBD)

Action: For adoption of advice to CHMP

7.6.7. Lopinavir, ritonavir - KALETRA (CAP) - EMEA/H/C/000368/LEG 121.1

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

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

7.8. Ongoing Scientific Advice

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. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/S/0023 (without RMP)

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Agni Kapou

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Cholic acid - ORPHACOL (CAP) - EMEA/H/C/001250/S/0026 (without RMP)

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sophia Trantza

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/S/0055 (with RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.5. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0023 (without RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.6. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/S/0047 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ghania Chamouni

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. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/R/0051 (with RMP)

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/R/0008 (without RMP)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Busulfan - BUSULFAN FRESENIUS KABI (CAP) - EMEA/H/C/002806/R/0010 (with RMP)

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/R/0063 (with RMP)

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/R/0036 (with RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/R/0049 (with RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ghania Chamouni

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Filgrastim - ACCOFIL (CAP) - EMEA/H/C/003956/R/0026 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/R/0049 (with RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Insulin degludec, liraglutide - XULTOPHY (CAP) - EMEA/H/C/002647/R/0028 (with RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Nintedanib - VARGATEF (CAP) - EMEA/H/C/002569/R/0025 (with RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Agni Kapou

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP) - EMEA/H/C/001206/R/0062 (with RMP)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

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. Duloxetine - CYMBALTA (CAP) - EMEA/H/C/000572/WS1527/0078/G; DULOXETINE LILLY (CAP) - EMEA/H/C/004000/WS1527/0014/G; XERISTAR (CAP) - EMEA/H/C/000573/WS1527/0081/G; YENTREVE (CAP) - EMEA/H/C/000545/WS1527/0063/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: PRAC consultation on the proposed product information amendments for the following grouped variations consisting of: 1) update of sections 4.4 and 4.6 of the SmPC in order to add a warning on the risk of postpartum haemorrhage based on the final results from study F1J-MC-B057 (listed as a category 3 study in the RMP): an observational study to assess maternal and foetal outcomes following exposure to duloxetine. The package leaflet is updated accordingly; 2) enrolment termination for study F1J-MC-B034 (study B034): pregnancy registry to compare the pregnancy and birth outcomes of women given duloxetine during pregnancy with those of an unexposed group of pregnant women. The RMP (version 13) is updated accordingly. In addition, the MAH took the opportunity to correct the term 'sucrase-isomaltase' in section 4.4 of the SmPC 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' and to bring the product information (PI) in line with the latest quality review of documents (QRD) template (version 10). Finally, the MAH proposed to combine into a single SmPC the Xeristar 30 mg SmPC, Xeristar 60 mg SmPC and the Yentreve 20 mg SmPC and Yentreve 40 mg SmPC respectively, following the policy on combined SmPCs (EMA/333423/2015)

See also 5.3.5.

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

11.2.1. Abciximab (NAP) - UK/H/PSUFU/00000014/201711

Applicant(s): Janssen Biologics B.V. (ReoPro)

PRAC Lead: Patrick Batty

Scope: PRAC consultation on a PSUR follow-up (PSU FU) procedure on the review of cases of profound delayed thrombocytopenia as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure on abciximab (PSUSA/00000014/201711) concluded in July 2018, on request of the United Kingdom

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 meeting dates 2020-2021 - amendment

Action: For discussion

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

PRAC lead: Martin Huber, Ulla Wändel Liminga, Menno van der Elst, Tatiana Magálová, Ghania Chamouni, Jan Neuhauser

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Healthcare Professionals Working Party (HCPWP) and Patients and Consumers Working Party (PCWP) - Nomination of PRAC representative(s)

Action: For discussion

12.4. Cooperation within the EU regulatory network

None

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

None

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q1 2019 and predictions

Action: For discussion

12.8.2. Marketing authorisation applications (MAA) forecast for 2019 – planning update dated Q1 2019

Action: For information

12.8.3. PRAC workload statistics – Q1 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. PRAC meeting highlights – proposal for revision

Action: For discussion

12.18.2. Public participation in pharmacovigilance

None

12.18.3. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Annex II conditions and specific obligations – process proposal for earlier review

Action: For adoption

12.20.2. Opioids abuse, misuse and dependence - establishment of an oversight group

PRAC lead: Ghania Chamouni

Action: For discussion

13. Any other business

14. Explanatory notes

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

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures
(Items 2 and 3 of the PRAC agenda)

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

Signals assessment and prioritisation
(Item 4 of the PRAC agenda)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.
The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.
The evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

Risk Management Plans (RMPs)
(Item 5 of the PRAC agenda)

The RMP describes what is known and not known about the side effects of a medicine and states how these risks will be prevented or minimised in patients. It also includes plans for studies and other activities to gain more knowledge about the safety of the medicine and risk factors for developing side effects.
RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available.

Assessment of Periodic Safety Update Reports (PSURs)
(Item 6 of the PRAC agenda)

A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.
PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

Post-authorisation Safety Studies (PASS)
(Item 7 of the PRAC agenda)

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

Product related pharmacovigilance inspections
(Item 9 of the PRAC agenda)

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

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