28 November 2016
EMA/PRAC/724425/2016
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 28 November-01 December 2016

Chair: June Raine – Vice-Chair: Almath Spooner

28 November 2016, 13:00 – 19:30, room 3/A

29 November 2016, 08:30 – 19:30, room 3/A

30 November 2016, 08:30 – 19:30, room 3/A

01 December 2016, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

15 December 2016, Time 09:00-12:00, room 7/B, via Adobe Connect

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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1. +Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held on 28 November-1 December 2016. See December 2016 PRAC minutes (to be published post January 2017 PRAC meeting).

1.2. Adoption of agenda of the meeting on 28 November–01 December 2016

Action: For adoption

1.3. Adoption of the minutes of the previous meeting on 24–27 October 2016

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

2.4. Planned public hearings

None

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

3.1. Newly triggered procedures

3.1.1. Lactose of bovine origin-containing medicinal products[1]: methylprednisolone (NAP) - EMEA/H/A-31/1449

Applicant: Pfizer Croatia d.o.o. (Solu-Medrol), various

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

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

Action: For adoption of a list of questions

3.2. Ongoing procedures

3.2.1. Gadolinium-containing contrast agents (GdCA): gadobenic acid (NAP); gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP); gadoversetamide – OPTIMARK (CAP) - EMEA/H/A-31/1437

Applicant: Mallinckrodt Deutschland GmbH (Optimark); various

PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Doris Stenver

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

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

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

Applicant: Eisai Ltd (Panretin, Targretin), various

PRAC Rapporteur: Leonor Chambel; PRAC Co-rapporteur: Julie Williams

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

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

3.3. Procedures for finalisation

3.3.1. Direct-acting antivirals (DAAV) indicated for the treatment of hepatitis C (interferon free): daclatasvir – DAKLINZA (CAP); dasabuvir – EXVIERA (CAP); ombitasvir,

[1] For intravenous (IV) or intramuscular (IM) use indicated for the treatment of acute allergic reactions only

paritaprevir, ritonavir – VIEKIRAX (CAP); simeprevir - OLYSIO (CAP); sofosbuvir – SOVALDI (CAP); sofosbuvir, ledipasvir – HARVONI (CAP) - EMEA/H/A-20/1438

Applicant: Bristol-Myers Squibb Pharma EEIG (Daklinza); AbbVie Ltd (Exviera, Viekirax); Janssen-Cilag International N.V. (Olysio); Gilead Sciences International Ltd (Harvoni, Sovaldi)

PRAC Rapporteur: Margarida Guimarães; PRAC Co-rapporteur: Dolores Montero Corominas

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

Action: For adoption of a recommendation to CHMP

3.4. Article 5(3) of Regulation (EC) No 726/2004 as amended: PRAC advice on CHMP request

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Albiglutide – EPERZAN (CAP)

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: Signal of acute kidney injury

Action: For adoption of PRAC recommendation

EPITT 18778 – New signal

Lead Member State: UK

4.1.2. Brentuximab vedotin – ADCETRIS (CAP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Signal of cytomegalovirus (CMV) reactivation

Action: For adoption of PRAC recommendation

EPITT 18789 – New signal

[2] 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

Lead Member State: NL

4.1.3. Daratumumab – DARZALEX (CAP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Leonor Chambel

Scope: Signal of tumour lysis syndrome (TLS)

Action: For adoption of PRAC recommendation

EPITT 18777 – New signal

Lead Member State: PT

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

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: To be appointed

Scope: Signal of sepsis

Action: For adoption of PRAC recommendation

EPITT 18779 – New signal

Lead Member States: SE, UK

4.1.5. Meropenem (NAP); ciprofloxacin (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of incompatibility leading to possible precipitation when co-administered intravenously

Action: For adoption of PRAC recommendation

EPITT 18790 – New signal

Lead Member State: AT

4.1.6. Pirfenidone – ESBRIET (CAP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Signal of colitis

Action: For adoption of PRAC recommendation

EPITT 18793 – New signal

Lead Member State: UK

4.1.7. Temozolomide – TEMODAL (CAP), NAP

Applicant: Merck Sharp & Dohme Limited; various

PRAC Rapporteur: Martin Huber

Scope: Signal of meningoencephalitis herpetic

Action: For adoption of PRAC recommendation

EPITT 18785 – New signal

Lead Member State: DE

4.2. New signals detected from other sources

4.2.1. Leflunomide – ARAVA (CAP); teriflunomide – AUBAGIO (CAP)

Applicant: Sanofi-aventis Deutschland GmbH (Arava), Sanofi-Aventis Groupe (Aubagio)

PRAC Rapporteur: To be appointed

Scope: Signal of falsely decreased ionised calcium levels

Action: For adoption of PRAC recommendation

EPITT 18787 – New signal

Lead Member States: DE, NL

4.3. Signals follow-up and prioritisation

4.3.1. Acenocoumarol (NAP), fluindione (NAP), phenindione (NAP), phenprocoumon (NAP)

Applicant: various

PRAC Rapporteur: Martin Huber

Scope: Signal of calciphylaxis

Action: For adoption of PRAC recommendation

EPITT 18710 – Follow-up to July 2016

4.3.2. Proton pump inhibitors (PPIs): dexlansoprazole (NAP); esomeprazole – NEXIUM CONTROL (CAP), NAP; lansoprazole (NAP);omeprazole (NAP); pantoprazole – CONTROLOC CONTROL (CAP), PANTECTA CONTROL (CAP), PANTOLOC CONTROL (CAP), PANTOZOL CONTROL (CAP), SOMAC CONTROL (CAP), NAP; rabeprazole (NAP)

Applicants: Pfizer Consumer Healthcare Ltd (Nexium Control), Takeda GmbH (Controloc Control, Pantecta Control, Pantoloc Control, Pantozol Control, Somac Control), various

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of gastric polyps

Action: For adoption of PRAC recommendation

EPITT 18725 – Follow-up to September 2016

4.3.3. Methylphenidate (NAP)

Applicant: various

PRAC Rapporteur: Julie Williams

Scope: Signal of priapism

Action: For adoption of PRAC recommendation

EPITT 18719 – Follow-up to July 2016

4.3.4. Vildagliptin - GALVUS (CAP) - EMEA/H/C/000771/SDA/043; JALRA (CAP) - EMEA/H/C/001048/SDA/027; XILIARX (CAP) - EMEA/H/C/001051/SDA/027 vildagliptin, metformin hydrochloride - EUCREAS (CAP) - EMEA/H/C/000807/SDA/025; ICANDRA (CAP) - EMEA/H/C/001050/SDA/023; ZOMARIST (CAP) - EMEA/H/C/001049/SDA/023

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of pemphigoid

Action: For adoption of PRAC recommendation

EPITT 18692 – Follow-up to July 2016

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Abaloparatide - EMEA/H/C/004157

Scope: Treatment of osteoporosis

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

5.1.2. Baricitinib - EMEA/H/C/004085

Scope: Treatment of moderate to severe active rheumatoid arthritis (RA)

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

5.1.3. Cerliponase alfa - EMEA/H/C/004065, Orphan

Applicant: BioMarin International Limited

Scope (accelerated assessment): Treatment of neuronal ceroid lipofuscinosis type 2

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

5.1.4. Fluciclovine (^{18}F) - EMEA/H/C/004197

Scope: Diagnostic agent for positron emission tomography (PET) of adult men with suspected recurrence of prostate cancer

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

5.1.5. Human immunoglobulin (Ig)G1 monoclonal antibody specific for human interleukin-1 alpha - EMEA/H/C/004388

Scope: Treatment of metastatic colorectal cancer

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

5.1.6. Ivabradine - EMEA/H/C/004241, Generic

Scope: Treatment of angina pectoris

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

5.1.7. Midostaurin - EMEA/H/C/004095, Orphan

Applicant: Novartis Europharm Ltd

Scope (accelerated assessment): Treatment of mastocytosis and acute myeloid leukaemia

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

5.1.8. Padeliporfin - EMEA/H/C/004182

Scope: Treatment of prostate cancer

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

5.1.9. Pemetrexed - EMEA/H/C/004488, Generic

Scope: Treatment of malignant pleural mesothelioma and non-small cell lung cancer (NSCLC)

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

5.1.10. Rurioctocog alfa pegol - EMEA/H/C/004195

Scope: Treatment of haemophilia A

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

5.1.11. Simoctocog alfa - EMEA/H/C/00459

Scope: Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)

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

5.1.12. Tofacitinib - EMEA/H/C/004214

Scope: Treatment of active rheumatoid arthritis (RA)

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

5.1.13. Vosaroxin - EMEA/H/C/004118, Orphan

Applicant: Sunesis Europe Ltd

Scope: Treatment acute myeloid leukaemia

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. Albiglutide - EPERZAN (CAP) - EMEA/H/C/002735/II/0028/G

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: Grouped variations including: 1) update of the RMP in order to introduce additional risk minimisation measures addressing the important potential risk of medication errors. Annex II of the Product Information is updated accordingly; 2) update of the RMP to add a new category 3 study as an additional pharmacovigilance activity - study 204879: a randomized, open-label, active-controlled, parallel-group, exploratory study on the effects of repeated doses of albiglutide compared to exenatide on gastric myoelectrical activity and gastric emptying in subjects with type 2 diabetes mellitus; 3) update of the RMP to add a new category 3 study as an additional pharmacovigilance activity - study 201840: an exploratory randomized, 2-part, single-blind, 2-period crossover study comparing the effect of albiglutide with exenatide on regional brain activity related to nausea in healthy volunteers; 4) update of the RMP to add a new category 3 study as an additional pharmacovigilance activity: cross-sectional survey to assess the effectiveness of the proposed additional educational materials using patient connect

Action: For adoption of PRAC Assessment Report

5.2.2. Antithrombin alfa - ATRYN (CAP) - EMEA/H/C/000587/II/0027

Applicant: GTC Biotherapeutics UK Limited

PRAC Rapporteur: Claire Ferard

Scope: Introduction of a RMP (version 1) as requested in the sixth annual re-assessment (EMEA/H/C/000587/S/0021) and second five-year renewal (EMEA/H/C/000587/R/0024)

Action: For adoption of PRAC Assessment Report

5.2.3. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/WS1063/0022; ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/WS1063/0027

Applicant: AbbVie Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update the RMP for Exviera and Viekirax to 1) add information on cases of hepatic decompensation observed in patients with Child-Pugh B hepatic impairment, and to the reflect the changes of the SmPC to change the dose recommendation of these patients to 'not recommended', as well as the addition of statements recommending the monitoring of hepatic function in these patients as approved on WS/0873; 2) add a reference to nine

drug-drug interaction studies as approved in WS0896/G; 3) include a reference to the completion of rat 2 year carcinogenicity studies as recently approved in variations II-06 (Exviera) and II-04 (Viekirax) respectively; 4) reflect the update of section 4.2 of SmPC for Viekirax to recommend a decrease in treatment duration of 12 weeks in genotype 4 (GT4) cirrhotic patients, with a consequential change to sections 4.4 and 5.1 as approved in II-22-G; 5) remove the non-clinical PAMS 1-3,(MEA/003, MEA/002, MEA/003)

Action: For adoption of PRAC Assessment Report

5.2.4. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/WS0953/0019; empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/WS0953/0019

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the RMP in order to reflect the outcome of the recently finalised procedure under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) including the addition of atypical DKA as an important identified risk for all sodium-glucose cotransporter-2 (SGLT2) inhibitors. In addition, ongoing and planned activities are being included in the RMP

Action: For adoption of PRAC Assessment Report

5.2.5. Eribulin - HALAVEN (CAP) - EMEA/H/C/002084/II/0033

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 4.2) to reflect the revised protocol for a post-authorisation study to capture data on the frequency of resolution and time to resolution of eribulin-induced or aggravated peripheral neuropathy from study E7389-A001-303 (ACCRU: a randomized phase III trial of eribulin compared to standard weekly paclitaxel as first- or second-line therapy for locally recurrent or metastatic breast cancer) to an observational post authorisation, single-arm, prospective multicentre cohort study E7389-M044-504 (IRENE). The submission of the corresponding study report to EMA remains unchanged and is planned in 2019

Action: For adoption of PRAC Assessment Report

5.2.6. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/II/0047

Applicant: Hospira UK Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Update of the RMP (version 7.0) to merge the RMPs for Remsima and Inflectra

Action: For adoption of PRAC Assessment Report

5.2.7. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/II/0039

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Rafe Suvarna

Scope: Update of the RMP (version 7.0) to merge the RMPs for Remsima and Inflectra

Action: For adoption of PRAC Assessment Report

5.2.8. Thyrotropin alfa - THYROGEN (CAP) - EMEA/H/C/000220/II/0088

Applicant: Genzyme Europe BV

PRAC Rapporteur: Almath Spooner

Scope: Update of the RMP to bring it in line with the latest RMP template. As a consequence, 'gastrointestinal symptoms', 'constitutional symptoms' and 'injection site reactions' are deleted resulting from their downgrade to identified risks as not categorized as important any longer. In addition, 'perceived lower thyroid-stimulating hormone (TSH) elevation after thyrotropin alfa administration' is deleted from the list of important potential risks as it does not correspond to a safety risk for patients treated with Thyrogen. Finally, the study results and completion date for the T4 study (collection of data about remnant ablation in patients originally diagnosed with T4 thyroid cancer) are added and as a consequence, use of Thyrogen for remnant ablation in patients originally diagnosed with T4N0-1M0-1 thyroid cancer' is removed as missing information. The RMP (version 9.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

5.3.1. Aliskiren - RASILEZ (CAP) - EMEA/H/C/000780/WS1026/0110; aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/WS1026/0080

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of section 5.1 of the SmPC in order to reflect the results of study SPP100F2301 (ATMOSPHERE): a multicentre, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II - IV). The RMP (version 13) is updated accordingly

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

5.3.2. Atazanavir sulfate - REYATAZ (CAP) - EMEA/H/C/000494/II/0105/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Claire Ferard

Scope: Grouped variations to: 1) update of section 4.6 of the SmPC in order to update the safety information on lactation to indicate that atazanavir has been detected in human milk. The Package Leaflet and the RMP are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet; 2) update of the RMP in order to add 'immune reconstitution inflammatory syndrome (IRIS)' and 'angioedema' as important identified risks and to update the epidemiology/exposure sections. The MAH also took the opportunity to make some reformatting changes to align

the RMP with the current approved EMA template

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

5.3.3. Bevacizumab - AVASTIN (CAP) - EMEA/H/C/000582/II/0092

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include the use of Avastin in combination with paclitaxel and carboplatin for the treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated with efficacy and safety information from study GOG-0213 (a phase III randomized controlled clinical trial of carboplatin and paclitaxel (or gemcitabine) alone or in combination with bevacizumab followed by bevacizumab and secondary cytoreductive surgery in platinum-sensitive, recurrent ovarian, peritoneal primary and fallopian tube cancer. nci-supplied agents: bevacizumab). The Package Leaflet and the RMP (version 27) are updated accordingly

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

5.3.4. C1-esterase inhibitor, human - CINRYZE (CAP) - EMEA/H/C/001207/II/0045

Applicant: Shire Services BVBA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include children with hereditary angioedema (HAE) in the treatment and pre-procedure prevention of angioedema attacks. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.5 of the SmPC are updated. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH proposed to update regional information in module 3.2.R due to the proposed dose recommendation for children

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

5.3.5. Canakinumab - ILARIS (CAP) - EMEA/H/C/001109/X/0045/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped application comprising a line extension covering an additional formulation (150 mg/ml solution for injection) and a type II variation to add a new indication based on the results of the pivotal phase 3 study CACZ885N2301 on the treatment of adults and children of 2 years of age and older with one of the following periodic fever syndromes: tumour necrosis factor receptor associated periodic syndrome (TRAPS); hyperimmunoglobulin D syndrome (HIDS), mevalonate kinase deficiency (MKD); familial Mediterranean fever (FMF) in patients in whom colchicine is contraindicated, is not tolerated, or does not provide an adequate response. As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 11) are updated accordingly. In addition, the annexes have been aligned with the latest QRD template (version 10)

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

5.3.6. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0054

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final clinical study report (CSR) for study AS001: a phase 3, multicentre, randomized, double-blind, placebo-controlled study to evaluate efficacy and safety of certolizumab pegol in subjects with active axial spondyloarthritis (axSpA). As a consequence, sections 4.8 and 5.1 of the SmPC are revised in order to update the efficacy and safety information (week 204) for study AS001. The RMP (version 11.0) is updated accordingly. The package leaflet remains unchanged

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

5.3.7. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0055

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final clinical study report (CSR) for study PsA001: a phase 3, multicentre, randomized, double-blind, parallel group, placebo-controlled study to evaluate the efficacy and safety of certolizumab pegol in subjects with adult onset active and progressive psoriatic arthritis (PsA), in order to provide data on long-term use of Cimzia in psoriatic arthritis subjects up to 216 weeks of treatment. As a consequence, sections 4.8 and 5.1 of the SmPC are revised in order to update the efficacy and safety information (week 216) for study PsA001. The RMP (version 11) is updated accordingly. The package leaflet remains unchanged

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

5.3.8. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0002

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Leonor Chambel

Scope: Extension of indication in the treatment of adult patients with multiple myeloma who have received at least 1 prior therapy. As a consequence, sections 4.2, 4.4, 4.5, 5.1 and 5.2 of the SmPC are updated in order to update the information on posology, warnings, interactions, efficacy and pharmacokinetics. A new warning is introduced in section 4.4 regarding neutropenia/thrombocytopenia induced by background therapy. Annex II is updated to remove all the specific obligations following submissions of the final results of studies MMY3003 (a phase III randomised study investigating lenalidomide and dexamethasone with or without daratumumab in patients with previously treated multiple myeloma) and MMY3004 (a phase III randomised study investigating bortezomib and dexamethasone with or without daratumumab in patients with previously treated multiple myeloma). The Package Leaflet and RMP (version 2) 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

5.3.9. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0057

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.6 of the SmPC in order to delete references to the pregnancy and lactation surveillance programmes. The Package Leaflet and the RMP are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial updates to the product information

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

5.3.10. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0062

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the sections 4.4 and 4.8 of the SmPC to update the safety information and reflect the possible occurrence of multiple vertebral fractures (MVF) particularly in patients with a history of vertebral fracture following discontinuation of Prolia treatment. This results from an analysis of osteoporosis-related fracture data in subjects who discontinued investigational product and remained on study in either the Prolia phase III pivotal fracture study (study 20030216: evaluation of denosumab in the treatment of postmenopausal osteoporosis FREEDOM (fracture reduction evaluation of denosumab in osteoporosis every 6 months)) or its study extension (study 20060289: open label, single arm, extension study to evaluate the long term safety and sustained efficacy of denosumab in the treatment of postmenopausal osteoporosis) to better understand the incidence of fracture following treatment discontinuation. The Package Leaflet is updated accordingly. The RMP is also updated to reflect MVF as a new important risk. In addition, the Product Information is updated in line with the QRD template latest version and corrected to remove typographical errors and implement minor changes in the list of local representatives

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

5.3.11. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0046

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.6 of the SmPC in order to delete references to the pregnancy and lactation surveillance programmes. The Package Leaflet and the RMP are updated accordingly. In addition, the MAH took the opportunity to make minor editorial updates to the product information

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

5.3.12. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0035

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to include ‘liver function abnormalities’ as an

adverse event observed in the post-marketing setting and to clarify events not observed in placebo-controlled studies. The Package Leaflet and the RMP (version 8) are updated accordingly. The MAH has also taken the opportunity to make minor administrative changes in the Package Leaflet

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

5.3.13. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/X/0018/G

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Grouped application comprising a line extension to add two new strengths (10 mg and 25 mg tablets) to support the extension of indication for the treatment of paediatric patients from 6 years of age infected with human immunodeficiency virus (HIV). Data from cohort I and II A of study ING112578 (a 48 week Phase 1/2 multicentre open-label non-comparative study to evaluate pharmacokinetic (PK), safety, tolerability and antiviral activity of dolutegravir in HIV-1 infected children and adolescents of 6 weeks to <18 years of age) are presented in support of the new therapeutic indication

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

5.3.14. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0086/G

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations including: 1) update of section 4.8 of the SmPC with the adverse drug reactions (ADR) frequencies to reflect overall exposure to eculizumab in clinical trials; 2) update of section 4.4 of the SmPC with warning and precautions on meningococcal vaccination timing as recommended by PRAC. The Package Leaflet, Annex II and the RMP (version 13) are updated accordingly. In addition, the RMP is updated in order to implement the previous PRAC recommendation to remove the off label use from missing information, to provide the exposure data from PSUR#13 and to update the epidemiology sections with more complete and recent scientific literature data. Moreover, the MAH took the opportunity to update the Product Information to add editorial changes and to bring it in line with the latest QRD template

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

5.3.15. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/II/0014

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication to include the prevention of cardiovascular events, based on the final data of the cardiovascular safety clinical trial EMPA-REG OUTCOME (a phase 3, multicentre, international, randomised, parallel group, double blind cardiovascular safety study of empagliflozin (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus patients with increased cardiovascular risk). As a consequence, section 4.1 of the SmPC is updated in order to add safety information on this study. The Package Leaflet is updated accordingly

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

5.3.16. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/WS0971/0022; empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/WS0971/0021

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final clinical report for study 1245.28 (4-year data) (a phase 3, randomised, double-blind, active controlled parallel group efficacy and safety study of empagliflozin compared to glimepiride administered orally during 104 weeks with a 104-week extension period in patients with type 2 diabetes mellitus and insufficient glycaemic control despite metformin treatment)

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

5.3.17. Eslicarbazepine acetate - ZEBINIX (CAP) - EMEA/H/C/000988/II/0053

Applicant: Bial - Portela & Cª, S.A.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include the use of Zebinix as monotherapy in adults, in addition to the previously authorised indication as adjunctive therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP (version 15.0) are updated accordingly

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

5.3.18. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/X/0016

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Rafe Suvarna

Scope: Line extension to add a new strength of 25 mg solution for injection in pre-filled syringe

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

5.3.19. Everolimus - VOTUBIA (CAP) - EMEA/H/C/002311/II/0041

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include the adjunctive treatment of patients aged 2 years and older with refractory seizures associated with tuberous sclerosis complex (TSC) for Votubia 2 mg, 3 mg and 5 mg dispersible tablets. Sections 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated based on the results from the pivotal study. In addition, sections 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 are also updated for the 2.5 mg, 5 mg and 10 mg tablets to reflect data relevant to these formulations. The Package Leaflet is updated accordingly. Furthermore, the Product Information is brought in line with the latest QRD template (version 10)

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

5.3.20. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/II/0004

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to include a warning and update the safety information as a result of a post-marketing case of hypertensive encephalopathy upon abrupt discontinuation of Intuniv (guanfacine hydrochloride). The Package Leaflet is updated accordingly

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

5.3.21. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - CERVARIX (CAP) - EMEA/H/C/000721/II/0085

Applicant: GSK Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of study EPI-HPV-069, a meta-analysis assessing the risk of three autoimmune diseases following vaccination with Cervarix: autoimmune thyroiditis (AIT), Guillain-Barre syndrome (GBS) and inflammatory bowel disease (IBD). The RMP (version 18) is updated accordingly, and includes minor updates related to other studies

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

5.3.22. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0029

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.5 of the SmPC to remove the statement that an interaction with medicinal products increasing stomach pH may decrease ibrutinib exposure and this has not as well as section 5.2 to include the findings from study CLL1005: an open-label, sequential-design drug interaction study of the effect of omeprazole on the pharmacokinetics of ibrutinib in healthy adults. The RMP (version 6.3) is updated accordingly. The Package Leaflet remains unchanged

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

5.3.23. Icatibant - FIRAZYR (CAP) - EMEA/H/C/000899/II/0034/G

Applicant: Shire Orphan Therapies GmbH

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variation including: 1) Extension of indication to include adolescents and children over 2 years old for the use of Firazyr for symptomatic treatment of acute attacks of hereditary angioedema. As a consequence, section 4.1, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6. of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to reflect the results of a juvenile toxicity study in SmPC section 5.3; 2) Update section 5.2 of the SmPC to reflect the effect of age (elderly), gender and race on pharmacokinetics of icatibant. The Package Leaflet is updated accordingly. All relevant pharmacokinetics studies have been previously assessed, as part of prior

submissions

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

5.3.24. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/II/0009

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final clinical study report (CSR) of study SB2-G31-RA: a randomised, double-blind, parallel group, multicentre clinical study to evaluate the efficacy, safety, pharmacokinetics and immunogenicity of Flixabi compared to Remicade in subjects with moderate to severe rheumatoid arthritis despite methotrexate therapy. The RMP (version 4) is updated to reflects the results from the 78 weeks CSR, to exclude 2 of the 5 registries of the pharmacovigilance plan and update the due date for the prospective observational cohort study of Flixabi in ankylosing spondylitis (AS) and Crohn's disease (CD) patients

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

5.3.25. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/II/0061

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.3 and 4.8 of the SmPC to reflect that Fluenz Tetra is contraindicated only in children with severe hypersensitivity to eggs (instead of all children with egg allergy), and to update the safety information by implementing the number of children and adolescents in the safety database. The Package Leaflet is updated accordingly. In addition, the RMP is updated to implement administrative changes to the high level description on enhanced safety surveillance (ESS) and to change the milestones for study MA-VA-MEDI3250-1116 (a case control study of the effectiveness of Fluenz Tetra versus inactivated influenza vaccine and no vaccine in subjects 2-17 years of age)

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

5.3.26. Ferric maltol - FERACCRU (CAP) - EMEA/H/C/002733/II/000002/G

Applicant: Shield TX (UK) Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of two final study reports for in vitro studies conducted as part of post-authorisation measures MEA 001 and MEA 002: 1) drug-drug interaction study to investigate drug interactions with Feraccru; 2) drug-drug interaction study to identify UGT isoenzyme(s) that are responsible for metabolism of ferric maltol. Consequential changes have been made to the RMP to reflect the completion of the studies

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

5.3.27. Levetiracetam - KEPPRA (CAP) - EMEA/H/C/000277/II/0162

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Update of section 4.8 of the SmPC in order to include acute kidney injury as an undesirable effect. The Package Leaflet is updated accordingly

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

5.3.28. Lixisenatide - LYXUMIA (CAP) - EMEA/H/C/002445/II/0020

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final clinical study report for study EFC12382, a randomized double-blind, placebo-controlled, 2 arm parallel group, multicentre study with a 24-week treatment period to assess the efficacy and safety of lixisenatide in patients with T2DM insufficiently controlled with basal insulin or without metformin, in order to fulfil MEA 004. In addition, the MAH took the opportunity to update the RMP (version 4.0) accordingly

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

5.3.29. Lopinavir, ritonavir - ALUVIA (Art 58[3]) - EMEA/H/W/000764/II/0100

Applicant: AbbVie Ltd.

PRAC Rapporteur: Claire Ferard

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to introduce the outcome from an analysis of the published 48-week study results PENTA 18/KONCERT: 'a Kaletra once daily randomised trial of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in human immunodeficiency virus (HIV)-1–infected children'. In addition, the RMP (version 8) is updated to remove the missing information safety concern of limited information of Aluvia 100 mg/25 mg film-coated tablets in the paediatric population

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

5.3.30. Lopinavir, ritonavir - KALETRA (CAP) - EMEA/H/C/000368/II/0160

Applicant: AbbVie Ltd.

PRAC Rapporteur: Claire Ferard

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to introduce the outcome from an analysis of the published 48-week study results PENTA 18/KONCERT: 'a Kaletra once daily randomised trial of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in human immunodeficiency virus (HIV)-1–infected children'. In addition, the RMP (version 8) is updated to remove the missing information safety concern of limited information of Kaletra 100 mg/25 mg film-coated tablets in the paediatric population

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

[3] Article 58 of Regulation (EC) No 726/2004 allows the Agency's 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)

5.3.31. Nilotinib - TASIGNA (CAP) - EMEA/H/C/000798/II/0087

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Submission of the final clinical study report (CSR) from study CAMN107A2132: a phase I, single centre, two group, open-label, non-randomized, drug-drug interaction study to evaluate the effects of nilotinib on the pharmacokinetics (PK) of valsartan in healthy volunteers (HV). The RMP (version 17) is updated accordingly

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

5.3.32. Nitisinone - ORFADIN (CAP) - EMEA/H/C/000555/II/0057

Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to amend the dosing frequency further to the results of a clinical pharmacology study NTBC-003: 'an open-label, non-randomized, sequential, multicentre study to evaluate the pharmacokinetics, efficacy and safety of once daily dosing compared to twice daily dosing of Orfadin in patients diagnosed with hereditary tyrosinemia type 1'. The Package Leaflet is updated accordingly

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

5.3.33. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0019

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy for Opdivo. As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the proposed indication, add a warning about the patient populations excluded from the clinical trial and update the safety information. 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

5.3.34. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0009/G

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Update of SmPC sections 4.2, 4.4, 4.8, 5.1 and 5.2 based on the results from study D5160C00003 (a phase III, open label, randomized study of Tagrisso versus platinum-based doublet chemotherapy for patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose disease has progressed with previous epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor therapy and whose tumours harbour a T790M mutation within the EGFR gene (AURA3)), the updated clinical study reports (CSR) for studies D5160C00001 (a phase II , open-label, multicentre study to assess the safety, tolerability, pharmacokinetics and anti-tumour activity of ascending

doses of Tagrisso in patients with advanced NSCLC who have progressed following prior therapy with an EGFR-tyrosine kinase inhibitor agent (AURAex)) and D5160C00002 (a phase II, open-label, single-arm study to assess the safety and efficacy of Tagrisso in patients with locally advanced/metastatic NSCLC whose disease has progressed with previous EGFR-tyrosine kinase inhibitor therapy and whose tumours are EGFR mutation and T790M mutation positive (AURA2)). The Package Leaflet and RMP (version 6.0) are updated accordingly. In addition, the MAH took the opportunity to make editorial changes in the SmPC and Package Leaflet. The provision of the CSR from study AURA3 addresses the Specific Obligation (SO) and hence the MAH requests the conversion from a conditional marketing authorisation (MA) to a full MA

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

5.3.35. Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/II/0031/G

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Julie Williams

Scope: Grouped variation to update section 4.8 of the SmPC with data on exposure and section 5.1 with information on maintenance of long-term efficacy based on clinical study data (study ATTAIN: a dose-frequency blinded, multicentre, extension study to determine the long-term safety and efficacy of pegylated interferon beta-1a (Plegridy) in subjects with relapsing multiple sclerosis). In addition, update of section 4.8 of the SmPC in order to add information concerning the onset and duration of flu-like symptoms based on clinical study data (study ALLOW: an open-label, two-arm randomized study to characterize flu-like symptoms in relapsing multiple sclerosis patients transitioning from current interferon beta therapies to Plegridy). The Package Leaflet and the RMP (version 3) are updated accordingly

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

5.3.36. Pirfenidone - ESBRIET (CAP) - EMEA/H/C/002154/X/0035/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Grouped application including a line extension to introduce a new pharmaceutical form associated with 3 new strengths (267mg, 534mg and 801mg film-coated tablets). In addition, manufacturing sites are also introduced for the currently approved 267mg hard capsules presentations (EU/1/11/667/001-003)

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

5.3.37. Rufinamide - INOVELON (CAP) - EMEA/H/C/000660/II/0037

Applicant: Eisai Ltd

PRAC Rapporteur: Claire Ferard

Scope: Extension of indication to include the treatment of seizures associated with Lennox-Gastaut syndrome in paediatric patients of 1 year of age and older, based on the results of study E2080-G000-303 (study 303): a randomized, controlled, open-label study to evaluate the cognitive development effects and safety, and pharmacokinetics of

adjunctive rufinamide treatment in paediatric subjects 1 to less than 4 years of age with inadequately controlled Lennox-Gastaut syndrome. This study was conducted to fulfil the long-term (2 years) safety and efficacy objectives required as part of the paediatric investigation plan (PIP) EMEA-000709-PIP01-09. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 9.0) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the annexes, to implement changes in line with the latest QRD template and to combine the SmPCs, labelling and Package Leaflets for the three authorised strengths of the tablet formulation in line with the current version of the QRD template

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

5.3.38. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0031

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information for melofibrosis following the completion of two 5-year follow up studies: INCB 18424-351 (randomized, double-blind, placebo-controlled study of the ruxolitinib tablets administered orally to subjects with primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis) and INC424A2352 (randomized study of ruxolitinib tablets compared to best available therapy in subjects with primary myelofibrosis, post-polycythemia vera-myelofibrosis or post-essential thrombocythemia myelofibrosis). Annex II is updated accordingly

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

5.3.39. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/II/0003

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Margarida Guimarães

Scope: Update of sections 4.4, 4.5 and 5.1 of the SmPC in order to reflect on emerging clinical data from study GS-US-342-1202 (a phase III, open-label study to investigate the efficacy and safety of sofosbuvir/velpatasvir fixed dose combination for 12 weeks in subjects with chronic hepatitis C virus (HCV) and human immunodeficiency virus (HIV)-1 coinfection). The RMP (version 1.0) is updated accordingly. In addition, minor administrative changes are implemented throughout the Product Information

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

5.3.40. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/II/0027/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations including: 1) submission of the final clinical study report (CSR) for study TDM4997g/BO25734 (TH3RESA study: a phase III randomized, multicentre, two arm, open-label trial to evaluate the efficacy of trastuzumab emtansine compared with treatment of physician's choice in patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer who have received at least two prior regimens of

HER2 directed therapy) to address the safety concerns of left ventricular dysfunction and safety in elderly patients. The RMP (version 6.0) and Annex II.D are updated accordingly; 2) update of the RMP following the submission of the third annual report of study H4621g (an observational study of pregnancy and pregnancy outcomes in women with breast cancer treated with Herceptin, Perjeta in combination with Herceptin, or Kadcyla during pregnancy or within 7 months prior to conception). The MAH took the opportunity to implement the following administrative changes to the RMP: inclusion of standard post-authorisation data based on PSUR#4; change of Herceptin picture in the Kadcyla educational material to align the picture with the recently approved version of the Herceptin vial label and carton

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

5.3.41. Travoprost - IZBA (CAP) - EMEA/H/C/002738/II/0005

Applicant: Alcon Laboratories (UK) Ltd

PRAC Rapporteur: Almath Spooner

Scope: Extension of indication to include treatment of paediatric patients aged 2 months to <18 years with ocular hypertension or paediatric glaucoma in order to decrease of elevated intraocular pressure (IOP). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package leaflet and the RMP (version 9.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor corrections in the SmPC and 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

5.3.42. Vemurafenib - ZELBORAF (CAP) - EMEA/H/C/002409/II/0037

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.5 of the SmPC in order to include information on drug-drug interaction with rifampicin. In addition, the MAH took the opportunity to update the RMP and to request modification of MEA 011 part 2 'study GO29475: a two-part steady-state interaction study with and rifampin (3YP3A4 inducer). Furthermore the MAH is requesting change of due dates for category 3 final study reports for studies GO29475 (MEA011), MO25515 (MEA006) and GP28492 (MEA010). The MAH is also including request for deletion from the RMP of the study 'phase I dose-escalation with efficacy tail extension study of vemurafenib in paediatric patients with surgically incurable and unresectable stage IIIC or stage IV melanoma harbouring BRAFV600 mutations (MEA 005)' to reflect the paediatric product specific waiver for treatment of melanoma as agreed with the PDCO on 24 April 2016

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Abiraterone - ZYTIGA (CAP) - PSUSA/00000015/201604

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Aclidinium bromide, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP); DUAKLIR GENUAIR (CAP) - PSUSA/00010307/201605

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alipogene tiparvovec - GLYBERA (CAP) - PSUSA/00010056/201604

Applicant: UniQure biopharma B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Anakinra - KINERET (CAP) - PSUSA/00000209/201605 (with RMP)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Apixaban - ELIQUIS (CAP) - PSUSA/00000226/201605

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Blinatumomab - BLINCYTO (CAP) - PSUSA/00010460/201605

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Jana Mladá

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Bortezomib - VELCADE (CAP) - PSUSA/00000424/201604

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Brinzolamide, timolol - AZARGA (CAP) - PSUSA/00000433/201604

Applicant: Alcon Laboratories (UK) Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Budesonide, formoterol - BIRESP SPIROMAX (CAP); BUDESONIDE/FORMOTEROL TEVA (CAP); BUDESONIDE/FORMOTEROL TEVA PHARMA B.V. (CAP); DUORESP SPIROMAX (CAP); VYLAER SPIROMAX (CAP) - PSUSA/00010202/201604

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Carbidopa, levodopa[4] - NUMIENT (CAP) - PSUSA/00010479/201605

Applicant: Impax Laboratories Netherlands BV

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Ceritinib - ZYKADIA (CAP) - PSUSA/00010372/201604

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

[4] Centrally authorised product only

Action: For adoption of recommendation to CHMP

6.1.12. Cetrorelix - CETROTIDE (CAP) - PSUSA/00000633/201604

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Cobicistat, darunavir - REZOLSTA (CAP) - PSUSA/00010315/201605

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - PSUSA/00010449/201605

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Dalbavancin - XYDALBA (CAP) - PSUSA/00010350/201605

Applicant: Durata Therapeutics International B.V.

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Decitabine - DACOGEN (CAP) - PSUSA/00009118/201605

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Delamanid - DELTYBA (CAP) - PSUSA/00010213/201604

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dihydroartemisinin, piperaquine tetraphosphate - EURARTESIM (CAP) - PSUSA/00001069/201604

Applicant: Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Efmoroctocog alfa - ELOCTA (CAP) - PSUSA/00010451/201605

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Fentanyl[5] - IONSYS (CAP) - PSUSA/00010453/201605

Applicant: Incline Therapeutics Europe Ltd

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Flutemetamol (^{18}F) - VIZAMYL (CAP) - PSUSA/00010293/201604

Applicant: GE Healthcare Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP); REVINTY ELLIPTA (CAP) - PSUSA/00010099/201605

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[5] Transdermal system - centrally authorised product only

6.1.23. Hemoprostol - MISOPROSTOL (Art 58[6]) – EMEA/H/W/002652/PSUV/0005

Applicant: Linepharma International Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Ibrutinib - IMBRUVICA (CAP) - PSUSA/00010301/201605

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Ivabradine - CORLENTOR (CAP); IVABRADINE ANPHARM (CAP); PROCORALAN (CAP) - PSUSA/00001799/201604

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

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Ketoconazole[7] - KETOCONAZOLE HRA (CAP) - PSUSA/00010316/201605

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Lidocaine, prilocaine[8] - FORTACIN (CAP) - PSUSA/00010110/201605

Applicant: Plethora Solutions Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Lumacaftor, ivacaftor - ORKAMBI (CAP) - PSUSA/00010455/201605

Applicant: Vertex Pharmaceuticals (Europe) Ltd

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

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Methylthioninium chloride - METHYLTHIONINIUM CHLORIDE PROVEBLUE (CAP) - PSUSA/00002029/201605

Applicant: Provepharm SAS

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Mycophenolate mofetil - CELLCEPT (CAP) - PSUSA/00002099/201605

Applicant: Roche Registration Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Necitumumab - PORTRAZZA (CAP) - PSUSA/00010471/201605

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Nintedanib[9] - VARGATEF (CAP) - PSUSA/00010318/201605

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Leonidas Klironomos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Obinutuzumab - GAZYVARO (CAP) - PSUSA/00010279/201604

Applicant: Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] Oncology indications only

6.1.34. Osimertinib - TAGRISSO (CAP) - PSUSA/00010472/201605

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP); prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - PREPANDRIX (CAP) - PSUSA/00002281/201605

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Pixantrone - PIXUVRI (CAP) - PSUSA/00009261/201605

Applicant: CTI Life Sciences Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Propranolol[10] - HEMANGIOL (CAP) - PSUSA/00010250/201604

Applicant: Pierre Fabre Dermatologie

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Radium (Ra^{223}) dichloride - XOFIGO (CAP) - PSUSA/00010132/201605

Applicant: Bayer Pharma AG

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Ramucirumab - CYRAMZA (CAP) - PSUSA/00010323/201604

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

[10] Centrally authorised product only

Action: For adoption of recommendation to CHMP

6.1.40. Retapamulin - ALTARGO (CAP) - PSUSA/00002622/201604

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Shingles (herpes zoster) vaccine (live) - ZOSTAVAX (CAP) - PSUSA/00009289/201605

Applicant: Sanofi Pasteur MSD SNC

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Siltuximab - SYLVANT (CAP) - PSUSA/00010254/201604

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Simeprevir - OLYSIO (CAP) - PSUSA/00010255/201605

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Sunitinib - SUTENT (CAP) - PSUSA/00002833/201604

Applicant: Pfizer Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Susoctocog alfa - OBIZUR (CAP) - PSUSA/00010458/201605

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Tafamidis - VYNDAQEL (CAP) - PSUSA/00002842/201605

Applicant: Pfizer Limited

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/201604

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.48. Tilmanocept - LYMPHOSEEK (CAP) - PSUSA/00010313/201605

Applicant: Navidea Biopharmaceuticals Limited

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Tolvaptan[11] - SAMSCA (CAP) - PSUSA/00002994/201605

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Turoctocog alfa - NOVOEIGHT (CAP) - PSUSA/00010138/201604

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Ulipristal[12] - ELLAONE (CAP) - PSUSA/00003074/201605

Applicant: Laboratoire HRA Pharma, SA

PRAC Rapporteur: Menno van der Elst

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

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Vedolizumab - ENTYVIO (CAP) - PSUSA/00010186/201605

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Telmisartan - KINZALMONO (CAP); MICARDIS (CAP); PRITOR (CAP); telmisartan, hydrochlorothiazide - KINZALKOMB (CAP); MICARDISPLUS (CAP); PRITORPLUS (CAP); NAP - PSUSA/00002882/201604

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

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Olanzapine - OLAZAX DISPERZI (CAP); ZALASTA (CAP); ZYPREXA (CAP); ZYPREXA VELOTAB (CAP); NAP - PSUSA/00002205/201603

Applicant: Glenmark Pharmaceuticals s.r.o. (Olazax Disperzi), Krka, d.d., Novo mesto (Zalasta), Eli Lilly Nederland B.V. (Zyprexa, Zyprexa Velotab), various

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Pramipexole - MIRAPEXIN (CAP); SIFROL (CAP); NAP - PSUSA/00002491/201604

Applicant: Boehringer Ingelheim International GmbH (Mirapexin, Sifrol), various

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Bacterial lysate of haemophilus influenzae, klebsiella pneumoniae, moraxella catarrhalis, staphylococcus aureus, streptococcus mitis, streptococcus pneumoniae, streptococcus pyogenes; bacterial lysate of haemophilus influenzae,

klebsiella pneumoniae, moraxella catarrhalis, staphylococcus aureus, streptococcus pneumoniae, streptococcus pyogenes (NAP) - PSUSA/00002786/201603

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Captopril, hydrochlorothiazide (NAP) - PSUSA/00000536/201604

Applicant: various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Ethinylestradiol, levonorgestrel (NAP) - PSUSA/00001309/201604

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Hydrochlorothiazide, quinapril (NAP) - PSUSA/00002592/201604

Applicant: various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Ivabradine, metoprolol (NAP) - PSUSA/00010381/201604

Applicant: various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Ivermectin[13] (NAP) - PSUSA/00010377/201604

Applicant: various

PRAC Lead: Claire Férard

Scope: Evaluation of a PSUSA procedure

[13] For systemic use only

Action: For adoption of recommendation to CMDh

6.3.7. Ivermectin[14] (NAP) - PSUSA/00010376/201604

Applicant: various

PRAC Lead: Claire Férard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Mycophenolic acid[15] (NAP) - PSUSA/00010243/201605

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. N(2)-L-alanyl-L-glutamine (NAP) - PSUSA/00003158/201603

Applicant: various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Paracetamol[16] (NAP) - PSUSA/00002311/201605

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Quinapril (NAP) - PSUSA/00002591/201604

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Risedronate (NAP) - PSUSA/00002648/201603

Applicant: various

PRAC Lead: Ulla Wändel Liminga

[14] For topical use only
[15] Apart from mycophenolate mofetil
[16] Intravenous (IV) formulation only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Thiopental (NAP) - PSUSA/00002929/201603

Applicant: various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Tobramycin[17] (NAP) - PSUSA/00009317/201603

Applicant: various

PRAC Lead: Margarida Guimarães

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Valganciclovir (NAP) - PSUSA/00003089/201603

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Carglumic acid - CARBAGLU (CAP) - EMEA/H/C/000461/LEG 032

Applicant: Orphan Europe S.A.R.L.

PRAC Rapporteur: Leonor Chambel

Scope: Cumulative review and analysis of cases of off-label use, lack of efficacy and medication errors as requested in the conclusions of procedure EMEA/H/C/PSUSA/00000564/201501 adopted by PRAC in September 2015

Action: For adoption of advice to CHMP

6.4.2. Eptotermin alfa – OPGENRA[18], OSIGRAFT[19]

Applicant: Olympus Biotech International Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Assessment of the final PSUR for eptotermin alfa following the conclusions of procedure PSUSA/00001247/201509 adopted by PRAC in May 2016 and following EC

[17] For ophthalmic and otic use only
[18] EC decision of MA withdrawal dated 30/06/2016
[19] EC decision of MA withdrawal dated 16/12/2015

decisions of MA withdrawal

Action: For information

6.4.3. Colesevelam - CHOLESTAGEL (CAP) - EMEA/H/C/000512/LEG 031.1

Applicant: Genzyme Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Review on improving the ease of administration of Chloestagel, due to the increased number of cases reporting 'drug administration error' between the two most recent PSURs, in particular cases where tablets were either crushed or cut as requested in the conclusions of EMEA/H/C/PSUSA/00000864/201503 adopted by PRAC in October 2015

Action: For adoption of advice to CHMP

6.4.4. Ingenol mebutate - PICATO (CAP) - EMEA/H/C/002275/LEG 008.1

Applicant: Leo Pharma A/S

PRAC Rapporteur: Julie Williams

Scope: MAH's response to LEG 008 [submission of a review relating to study LP0105-1020[20] (efficacy and safety of ingenol mebutate gel 0.06% when applied once daily for 2, 3 or 4 consecutive days to a treatment area of approximately 250 cm^2 on trunk and extremities in subjects with actinic keratosis) as requested in the conclusions of PSUSA/00010035/201507] as per the request for supplementary information (RSI) adopted in July 2016

Action: For adoption of advice to CHMP

6.4.5. Omalizumab - XOLAIR (CAP) - EMEA/H/C/000606/LEG 050.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: The MAH's response to LEG 050.1 [venous thromboembolism (VTE) cumulative review as requested in the conclusions of EMEA/H/C/PSUSA/00002214/201412 adopted by the PRAC in July 2015] as per the request for supplementary information (RSI) adopted in May 2016

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[21]

7.1.1. Brentuximab vedotin – ADCETRIS (CAP) - EMEA/H/C/PSA/0009

Applicant: Takeda Pharma A/S

[20] Efficacy and safety of ingenol mebutate gel 0.06% when applied once daily for 2, 3 or 4 consecutive days to a treatment area of approximately 250 cm^2 on trunk and extremities in subjects with actinic keratosis. NCT01998984

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

PRAC Rapporteur: Sabine Straus

Scope: Submission of an amended PASS protocol for study MA25101: an observational cohort study of the safety of brentuximab vedotin in the treatment of relapsed or refractory CD30+ Hodgkin lymphoma and relapsed or refractory systemic anaplastic large cell lymphoma (sALCL) (study referenced in SOB 008 and SOB 009; initial protocol endorsed by PRAC in May 2014 (EMEA/H/C/002455/SOB 008))

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

7.1.2. Eliglustat – CERDELGA (CAP) - EMEA/H/C/PSP/S/0047.1

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: Revised PASS protocol for registry study OBS14099: a prospective, multicentre, observational post authorisation safety sub-registry to characterize the long-term safety profile of eliglustat of adult patients with Gaucher disease as per the request for supplementary information (RSI) adopted at PRAC in July 2016

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

7.1.3. Glycerol phenylbutyrate – RAVICTI (CAP) - EMEA/H/C/PSP/S/0048.1

Applicant: Horizon Pharma Ireland Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: Revised PASS protocol for a multicentre prospective non-interventional registry in patients with urea cycle disorders on treatment with glycerol phenylbutyrate to characterise patients' demographics, and to document long-term safety and clinical outcomes as per the request for supplementary information (RSI) adopted at PRAC in July 2016

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

7.1.4. Levofloxacin – QUINSAIR (CAP) - EMEA/H/C/PSP/S/0049.1

Applicant: Raptor Pharmaceuticals Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Revised PASS protocol for an open-label, observational safety study of Quinsair (nebulised levofloxacin hemihydrate) in patients with cystic fibrosis and chronic *Pseudomonas Aeruginosa* infection, using data collected through European cystic fibrosis registries as per the request for supplementary information (RSI) adopted at PRAC in July 2016

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

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

7.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.1

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Revised PASS protocol for study OBS13434: a prospective, multicentre, observational, PASS to evaluate the long term safety profile of alemtuzumab treatment in patients with relapsing forms of multiple sclerosis (RMS) as per the request for supplementary information (RSI) adopted in May 2016

Action: For adoption of advice to CHMP

7.2.2. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 019.1

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 019 [Protocol for a drug utilisation study (DUS) of alirocumab in Europe to assess the effectiveness of the dosing recommendation to avoid very low low-density lipoprotein (LDL)-C levels (study OBS14697)] as per the request for supplementary information (RSI) adopted in July 2016

Action: For adoption of advice to CHMP

7.2.3. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 007

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Submission of a non-clinical mechanistic study protocol in dogs to investigate the mechanism behind canagliflozin-containing medicines induced diabetic ketoacidosis occurrence, as per the outcome of the recently finalised procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA)

Action: For adoption of advice to CHMP

7.2.4. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 008

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Retrospective, observational cohort study protocol, using 4 administrative claims databases, to assess the incidence of diabetic ketoacidosis among patients with Type 2 diabetes mellitus treated with canagliflozin-containing medicines or other antihyperglycemic agents

Action: For adoption of advice to CHMP

[22] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

7.2.5. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 006

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Non-clinical mechanistic study protocol in dogs to investigate the mechanism behind canagliflozin-containing medicines induced diabetic ketoacidosis occurrence, as an outcome of the recently finalised procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA)

Action: For adoption of advice to CHMP

7.2.6. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 007

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Retrospective, observational cohort study protocol, using administrative claims databases, to assess the incidence of diabetic ketoacidosis among patients with type 2 Diabetes Mellitus treated with canagliflozin-containing medicines or other antihyperglycemic agents.

Action: For adoption of advice to CHMP

7.2.7. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/MEA 001

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Leonor Chambel

Scope: PASS protocol for study entitled 'survey of the effectiveness of Darzalex educational materials regarding the minimisation of risk of interference for blood typing with daratumumab'

Action: For adoption of advice to CHMP

7.2.8. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/MEA 067

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: PASS protocol and questionnaire for a cross sectional physician survey (study N6987) to assess the impact of educational materials on prescribers' awareness of doses and biological monitoring recommendations and also to assess the awareness and appropriate use of both formulations (orodispersible tablets and film-coated tablets) as requested as part of X/43 (category 3 study in the RMP)

Action: For adoption of advice to CHMP

7.2.9. Migalastat - GALAFOLD (CAP) - EMEA/H/C/004059/MEA 001

Applicant: Amicus Therapeutics UK Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol for a registry: prospective, multicentre, multinational, observational disease registry in Fabry disease patients treated with migalastat and untreated patients) to evaluate the long-term safety and effectiveness of migalastat in Fabry disease patients in real-world setting

Action: For adoption of advice to CHMP

7.2.10. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/MEA 011.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: MAH's response to MEA 011.3 [revised protocol for a PASS to collect and/or retrieve prospective data from sizeable patient cohorts with ovarian cancer (Study D0816R00008b)] as per request for supplementary information (RSI) adopted in July 2016

Action: For adoption of advice to CHMP

7.2.11. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 003

Applicant: Actelion Registration Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: PASS protocol for a study to evaluate risk minimisation measures for mEDication errors with Uptravi during the titration phase in patients with pulmonary arterial hypertension (PAH) in Clinical prAcTicE (EDUCATE), protocol number: AC-065A403 version 1

Action: For adoption of advice to CHMP

7.2.12. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/MEA 025

Applicant: Shire Pharmaceuticals Ireland Ltd.

PRAC Rapporteur: Valerie Strassmann

Scope: PASS protocol to evaluate the effectiveness of risk minimisation measures: a survey among healthcare professionals and patient/caregivers to assess their knowledge and attitudes on prescribing and home administration conditions of velaglucerase alfa in 6 European countries as per the conclusions of variation EMEA/H/C/001249/II/0029 dated April 2016

Action: For adoption of advice to CHMP

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

7.3.1. Cyproterone, ethinylestradiol (NAP) - EMEA/H/N/PSR/J/0003.1

Applicant: Bayer Pharma AG, various

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study results on the drug utilisation study (DUS) (database)

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

designed to characterize the prescribing behaviours for cyproterone acetate/ethinylestradiol (CPA/EE) in three European countries: Netherlands, United Kingdom and Italy

Action: For adoption of a recommendation to CMDh

7.3.2. Cyproterone, ethinylestradiol (NAP) - EMEA/H/N/PSR/J/0005.1

Applicant: Bayer Pharma AG, various

PRAC Rapporteur: Menno van der Elst

Scope: Final study results on the drug utilisation study (DUS) (survey) designed to characterize the prescribing behaviours for cyproterone acetate/ethinylestradiol (CPA/EE) in five European countries: Austria, Czech Republic, France, the Netherlands, and Spain

Action: For adoption of a recommendation to CMDh

7.3.3. Cyproterone, ethinylestradiol (NAP) - EMEA/H/N/PSR/J/0006.1

Applicant: Bayer Pharma AG, various

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study results on the PASS to evaluate the effectiveness of the risk minimisation activities with the objective to measure physicians' knowledge of safety and safe use information for cyproterone acetate/ethinylestradiol (CPA/EE) in five European countries: Austria, the Czech Republic, France, the Netherlands, and Spain

Action: For adoption of a recommendation to CMDh

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

7.4.1. Agomelatine - THYMANAX (CAP) - EMEA/H/C/000916/II/0031; VALDOXAN (CAP) - EMEA/H/C/000915/II/0033

Applicant: Servier (Ireland) Industries Ltd, Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Submission of the final study report for study CLE-20098-095: 'HLA alleles as genetic risk factors for elevation of aminotransferase levels in patients treated with agomelatine'. The product information and RMP remain unchanged

Action: For adoption of PRAC Assessment Report

7.4.2. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/II/0093

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of the final clinical study report for PASS 1160.149: observational study to evaluate the effectiveness of the risk minimisation activities in the treatment of stroke prevention in atrial fibrillation (SPAF) in order to address part of follow-up measure MEA

[24] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

026. The RMP (version 31.6) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP) - EMEA/H/C/002673/WS1028/0027; REVINTY ELLIPTA (CAP) - EMEA/H/C/002745/WS1028/0023

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of study HZA107112 (a randomised, double-blind, two-way crossover study to investigate the effect of inhaled fluticasone furoate on short-term lower-leg growth in paediatric subjects with asthma) to investigate the important potential risk of growth retardation in children. This study was conducted as part of the paediatric investigational plan (EMEA-000431-PIP01-08). In addition, the RMP (version 8.2) is updated to amend the due date for drug utilisation study 205052

Action: For adoption of PRAC Assessment Report

7.4.4. Lixisenatide - LYXUMIA (CAP) - EMEA/H/C/002445/II/0019

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final clinical study report (CSR) for a non-interventional PASS: a retrospective database study of glucagon-like peptide-1 (GLP-1) receptor agonists and risk of acute pancreatitis, pancreatic cancer and thyroid cancer in particular medullary thyroid cancer, a category 3 study in order to fulfil MEA 007.2

Action: For adoption of PRAC Assessment Report

7.4.5. Olanzapine - ZYPADHERA (CAP) - EMEA/H/C/000890/II/0032

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final study report of the PASS: post-injection syndrome in patients with schizophrenia receiving olanzapine long-acting injection. The RMP (version 12) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Regadenoson - RAPISCAN (CAP) - EMEA/H/C/001176/II/0023

Applicant: Rapidscan Pharma Solutions EU Ltd.

PRAC Rapporteur: Julie Williams

Scope: Submission of study report 01-1-401 to assess the safety profile of Rapiscan (regadenoson) in patients with liver impairment and to observe common adverse events reported in the post marketing setting

Action: For adoption of PRAC Assessment Report

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

7.5.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 046.6

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Seventh annual interim report of the registry in juvenile idiopathic arthritis (JIA) patients (P10-262: a long-term, multicentre, longitudinal post-marketing, observational study to assess long term safety and effectiveness of Humira (adalimumab) in children with moderately to severely active polyarticular or polyarticular-course JIA - STRIVE) (due date: final registry report 31 December 2021)

Action: For adoption of advice to CHMP

7.5.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 065.6

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Seventh annual interim report from the psoriasis patient registry (study P10-023: a 10-year, post-marketing, observational study to assess long term safety of Humira (adalimumab) in adult patients with chronic plaque psoriasis (PS)) (due date: final registry report by end of February 2023)

Action: For adoption of advice to CHMP

7.5.3. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 075.5

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of advice to CHMP

7.5.4. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 080.4

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second Annual Interim Report (P11-292 registry) from ‘a long-term non-interventional registry to assess safety and effectiveness of Humira (adalimumab) in paediatric patients with moderately to severely active Crohn’s disease (CD) CAPE’

Action: For adoption of advice to CHMP

7.5.5. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 056.1

Applicant: Genzyme Europe BV

PRAC Rapporteur: Claire Ferard

Scope: Interim report from a healthcare pofessional survey that measure the effectiveness of the approved safety information packet (SIP)

Action: For adoption of advice to CHMP

7.5.6. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.1

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: MAH's response to MEA 002 on the interim report for a long-term observational study of ataluren safety and effectiveness in usual care (protocol PTC124-GD-025o-DMD)] as per the request for supplementary information (RSI) adopted in July 2016

Action: For adoption of advice to CHMP

7.5.7. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/MEA 011.4

Applicant: Pfizer Limited

PRAC Rapporteur: Claire Ferard

Scope: Second interim report for study A8081038 to estimate the incidence rate and incidence proportion over a 3-year period of observation for hepatotoxicity, pneumonitis/interstitial lung disease (ILD), QTc prolongation related events, bradycardia, and visual disorder among lung cancer patients receiving crizotinib prescriptions as per the request for supplementary information (RSI) adopted by PRAC and CHMP in September 2015

Action: For adoption of advice to CHMP

7.5.8. Data collection on adverse events of anti-HIV[25] drugs (D:A:D) study - PRAC evaluation of D:A:D data merger results

Applicant: various

PRAC Representatives: Filip Josephson, Deborah Ashby

Scope: Evaluation of the sixteenth data merger

Action: For adoption of advice to CHMP

7.5.9. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/MEA 004

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Progress report for study GENA-99: prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice

Action: For adoption of advice to CHMP

[25] Human immunodeficiency virus

7.6. Others

7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 009

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Feasibility assessment to evaluate the drug utilisation patterns of canagliflozin-containing medicines including off-label usage in Type 1 Diabetes Mellitus, using 3 EU databases (United Kingdom, Spain and Italy)

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 008

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Feasibility assessment to evaluate the drug utilisation patterns of canagliflozin-containing medicines including off-label usage in type 1 diabetes mellitus, using 3 EU databases (United Kingdom, Spain and Italy)

Action: For adoption of advice to CHMP

7.6.3. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 008

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Feasibility assessment regarding prospective plasma hormone sampling (e.g. insulin, glucagon and incretin) in new or ongoing clinical trials, as an outcome of the recently finalised procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA)

Action: For adoption of advice to CHMP

7.6.4. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 005

Applicant: Boehringer Ingelheim GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Feasibility assessment regarding prospective plasma hormone sampling (e.g. insulin, glucagon and incretin) in new or ongoing clinical trials, as an outcome of the recently finalised procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA)

Action: For adoption of advice to CHMP

7.6.5. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/MEA 026

Applicant: Shire Pharmaceuticals Ireland Ltd.

PRAC Rapporteur: Valerie Strassmann

Scope: Update of RMP Annex 7 (inclusion of the updated Laboratory test requisition form for antibody testing as per conclusions EMEA/H/C/001249/II/0029 dated 28 April 2016)

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Antithrombin alfa - ATRYN (CAP) - EMEA/H/C/000587/S/0028 (without RMP)

Applicant: GTC Biotherapeutics UK Limited

PRAC Rapporteur: Claire Ferard

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/003794/S/0011 (without RMP)

Applicant: Alexion Europe SAS

PRAC Rapporteur: Almath Spooner

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/S/0065 (without RMP)

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Rafe Suvarna

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. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/R/0023 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/R/0023 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Docetaxel - DOCETAXEL ACCORD (CAP) - EMEA/H/C/002539/R/0030 (without RMP)

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Claire Ferard

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Docetaxel - DOCETAXEL KABI (CAP) - EMEA/H/C/002325/R/0015 (with RMP)

Applicant: Fresenius Kabi Oncology Plc

PRAC Rapporteur: Claire Ferard

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Follitropin alfa, lutropin alfa - PERGOVERIS (CAP) - EMEA/H/C/000714/R/0050 (without RMP)

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/R/0091 (without RMP)

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Pioglitazone - PIOGLITAZONE TEVA (CAP) - EMEA/H/C/002297/R/0016 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Pioglitazone - PIOGLITAZONE TEVA PHARMA (CAP) - EMEA/H/C/002410/R/0013 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

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

Scope: Pharmacovigilance inspection programme 2016-2019 (second revision for 2016)

Action: For adoption

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/003794/II/0008

Applicant: Alexion Europe SAS

PRAC Rapporteur: Almath Spooner

Scope: PRAC consultation on a variation to update sections 4.4 and 4.8 of the SmPC in order to reinforce the wording on the risk of anaphylaxis. The Package Leaflet is updated accordingly. The MAH took the opportunity to include the pharmacotherapeutic group in section 5.1

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

10.1.2. Ponatinib – ICLUSIG (CAP) - EMEA/H/C/002695/II/0032/G

Applicant: Incyte Biosciences UK Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: PRAC consultation on a variation to update sections 4.2, 4.4, 4.8, 5.1 of the SmPC based on data from ongoing study AP24534-07-101 with a median duration of follow-up of approximately 48 months for the CP-chronic myeloid leukaemia (CML) patients and 3.6 months for the advanced phase Ph+ leukemia patients, as well as 48-month follow-up data from the ongoing study AP24534-10-201 (PACE) (dose reduction advice as previously agreed by PRAC in the procedure under Article 20 of Regulation (EC) No 726/2004 finalised in 2014). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and to align the annexes with the latest QRD template (version 10)

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

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. Chlormadinone, ethinyl estradiol (NAP)

Applicant: Gedeon Richter, various

PRAC Lead: Valerie Strassmann

Scope: PRAC consultation on the revised statistical analysis plan (SAP) for an imposed PASS comparing the risk of venous thromboembolism (VTE) with chlormadinone/ethinyestradiol (CMA/EE) versus levonorgestrel/ethinylestradiol (LVG/EE) following the PRAC endorsement in January 2016 of its protocol (EMEA/H/N/PSP/j/0012.3), as per the conclusions of the review under Article 31 of Directive 2001/83/EC on combined hormonal contraceptive (CHC) (EMA/607314/2013)

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) steering group - nomination of PRAC representative for 2017-2019

Action: For adoption

12.4.2. Pharmacovigilance operation - EU training curriculum design document

PRAC lead: Margarida Guimarães

Action: For adoption

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

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Good Pharmacovigilance Practices (GVP) module II - Pharmacovigilance system master file – Revision 2

Action: For discussion

12.9.2. Pharmacovigilance systems and their quality systems

None

12.9.3. Pharmacovigilance inspections

None

12.9.4. 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, Margarida Guimarães

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Sabine Straus

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Good Pharmacovigilance Practice (GVP) Module V on risk management systems – Revision 2

Action: For adoption

12.14.2. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public hearings - procedural and best practice guidance for PRAC members

PRAC Lead: Albert van der Zeijden

Action: For discussion

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Good Pharmacovigilance Practices (GVP) – revised PRAC process for GVP modules in 2016/2017 - update on GVP status overview

Action: For discussion

12.20.2. Policy on handling competing interests for scientific committees' members and experts - update

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/