09 March 2020
EMA/PRAC/78004/2020
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 09-12 March 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

09 March 2020, 13:00 – 19:30, room 1/C

10 March 2020, 08:30 – 19:30, room 1/C

11 March 2020, 08:30 – 19:30, room 1/C

12 March 2020, 08:30 – 16:00, room 1/C

Organisational, regulatory and methodological matters (ORGAM)

26 March 2020, 09:00 – 12:00, room 1/F, via teleconference

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held on 09–12 March 2020. See March 2020 PRAC minutes (to be published post April 2020 PRAC meeting).

1.2. Agenda of the meeting on 09-12 March 2020

Action: For adoption

1.3. Minutes of the previous meeting on 10-13 February 2020

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

3.1.1. Ifosfamide[1] (NAP) - EMEA/H/A-31/1495

Applicant(s): various

[1] Solution, concentrate for solution

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

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

Action: For adoption of a list of questions (LoQ)

3.1.2. Ulipristal acetate – ESMYA (CAP); NAP - EMEA/H/A-31/1496

Applicant(s): Gedeon Richter Plc.; various

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

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 questions (LoQ)

3.2. Ongoing procedures

3.2.1. Leuprorelin[2] (NAP) - EMEA/H/A-31/1486

Applicant(s): various

PRAC Rapporteur: Željana Margan Koletić; PRAC Co-rapporteur: Eva Segovia

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

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

3.3. Procedures for finalisation

3.3.1. Fluorouracil and related substances: capecitabine - CAPECITABINE ACCORD (CAP); CAPECITABINE MEDAC (CAP); CAPECITABINE TEVA (CAP); ECANSYA (CAP); XELODA (CAP); NAP flucytosine (NAP); 5-fluorouracil (5-FU) (NAP); tegafur (NAP); tegafur, gimeracil, oteracil – TEYSUNO (CAP) - EMEA/H/A-31/1481

Applicants: Accord Healthcare Limited (Capecitabine Accord), Krka, d.d., Novo mesto (Ecansya), Medac Gesellschaft fur klinische Spezialpraparate mbH (Capecitabine medac), Nordic Group B.V. (Teysuno), Roche Registration GmbH (Xeloda), Teva B.V. (Capecitabine Teva), various

PRAC Rapporteur: Jean-Michel Dogné; PRAC Co-rapporteur: Martin Huber

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

Action: For adoption of a recommendation to CHMP

[2] Depot formulation(s)

3.4. Re-examination procedures[3]

None

3.5. Others

None

4. Signals assessment and prioritisation[4]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Apixaban – ELIQUIS (CAP)

Applicant(s): Bristol-Myers Squibb, Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Signal of erythema multiforme

Action: For adoption of PRAC recommendation

EPITT 19534 – New signal

Lead Member State(s): NL

4.1.2. Dabigatran – PRADAXA (CAP)

Applicant(s): Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of gastro-oesophagitis

Action: For adoption of PRAC recommendation

EPITT 19530 – New signal

Lead Member State(s): DK

4.1.3. Lamotrigine (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of photosensitivity

Action: For adoption of PRAC recommendation

[3] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[4] 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

EPITT 19548 – New signal

Lead Member State(s): NL

4.2. New signals detected from other sources

4.2.1. Amitriptyline (NAP); bupropion (NAP); citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); mirtazapine (NAP); paroxetine (NAP); sertraline (NAP); trazodone (NAP); venlafaxine (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of post-partum haemorrhage

Action: For adoption of PRAC recommendation

EPITT 19552 – New signal

Lead Member State(s): FR, GR, LT, NL, SE

4.2.2. Lopinavir, ritonavir – ALUVIA (Art 58[5]), KALETRA (CAP), LOPINAVIR/RITONAVIR MYLAN (CAP); NAP

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Aluvia, Kaletra), Mylan S.A.S (Lopinavir, Ritonavir Mylan), various

PRAC Rapporteur: To be appointed

Scope: Signal of adrenal dysfunction in infants

Action: For adoption of PRAC recommendation

EPITT 19527 – New signal

Lead Member State(s): FR

4.2.3. Interferon alfa-2a (NAP); interferon alfa-2b - INTRONA (CAP); peginterferon alfa-2a – PEGASYS (CAP); peginterferon alfa-2b - PEGINTRON (CAP), VIRAFERONPEG (CAP)

Applicant(s): Merck Sharp & Dohme B.V. (IntronA, PegIntron, ViraferonPeg); Roche Registration GmbH (Pegasys), various

PRAC Rapporteur: To be appointed

Scope: Signal of neuromyelitis optica spectrum disorder

Action: For adoption of PRAC recommendation

EPITT 19532 – New signal

Lead Member State(s): BE, NL, SE

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

4.3. Signals follow-up and prioritisation

4.3.1. Buprenorphine – BUVIDAL (CAP), SIXMO (CAP), NAP; buprenorphine, naloxone – SUBOXONE (CAP), ZUBSOLV (CAP), NAP; Selective serotonin reuptake inhibitors (SSRIs): citalopram (NAP); escitalopram (NAP); fluvoxamine (NAP); fluoxetine (NAP); paroxetine (NAP); sertraline (NAP); Serotonin norepinephrine reuptake inhibitors (SNRIs): desvenlafaxine (NAP); duloxetine – CYMBALTA (CAP), DULOXETINE LILLY (CAP), DULOXETINE MYLAN (CAP), DULOXETINE ZENTIVA (CAP), XERISTAR (CAP), YENTREVE (CAP), NAP; milnacipran (NAP); venlafaxine (NAP); Tricyclic antidepressants (TCAs): amitriptyline (NAP); clomipramine (NAP); doxepin (NAP); imipramine (NAP); nortriptyline (NAP); trimipramine (NAP); Monoamine oxidase inhibitors (MAOIs): isocarboxazid (NAP); phenelzine (NAP); selegiline (NAP); tranylcypromine (NAP); Other psychiatric medicines: amoxapine (NAP); buspirone (NAP); lithium (NAP); maprotiline (NAP); mirtazapine (NAP); trazodone (NAP); Serotonin receptor agonists: almotriptan (NAP); frovatriptan (NAP); naratriptan(NAP); rizatriptan (NAP); sumatriptan (NAP); zolmitriptan (NAP); Antiemetics: granisetron - SANCUSO (CAP), NAP; ondansetron (NAP); palonosetron – ALOXI (CAP), PALONOSETRON ACCORD (CAP), NAP; netupitant, palonosetron – AKYNZEO (CAP); tropisetron (NAP); Other serotonergic drugs: cyclobenzaprine (NAP); dextromethorphan (NAP); hypericum perforatum (NAP); linezolid (NAP); methylene blue (NAP); tryptophan (NAP)

Applicant(s): Accord Healthcare S.L.U. (Palonosetron Accord), Camurus AB (Buvidal), Eli Lilly Nederland B.V. (Cymbalta, Duloxetine Lilly, Xeristar, Yentreve), Helsinn Birex Pharmaceuticals (Aloxi, Akynzeo), Indivior Europe Limited (Suboxone), Kyowa Kirin Holdings B.V. (Sancuso), L. Molteni & C. dei Fratelli Alitti (Sixmo), Mundipharma Corporation (Nyxoid), Mylan S.A.S (Duloxetine Mylan), Orexo AB (Zubsolv), Zentiva k.s. (Duloxetine Zentiva), various

PRAC Rapporteur: Martin Huber

Scope: Signal of drug-drug interaction with serotonergic drugs leading to serotonin syndrome

Action: For adoption of PRAC recommendation

EPITT 19475 – Follow-up to November 2019

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

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

PRAC Rapporteur: Menno van der Elst

Scope: New information on the known risk of breast cancer

Action: For adoption of PRAC recommendation

EPITT 19482 – Follow-up to January 2020

4.3.3. Immune checkpoint inhibitors: atezolizumab – TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/018.1; avelumab – BAVENCIO (CAP) - EMEA/H/C/004338/SDA/005; cemiplimab – LIBTAYO (CAP) EMEA/H/C/004844/SDA/004.1; durvalumab – IMFINZI (CAP) EMEA/H/C/004771/SDA/003.1; ipilimumab – YERVOY (CAP) EMEA/H/C/002213/SDA/039; nivolumab – OPDIVO (CAP) EMEA/H/C/003985/SDA/039; pembrolizumab - KEYTRUDA (CAP) EMEA/H/C/003820/SDA/024

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

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of tuberculosis

Action: For adoption of PRAC recommendation

EPITT 19464 – Follow-up to January 2020

4.3.4. Mycophenolic acid (NAP); mycophenolate mofetil - CELLCEPT (CAP) - EMEA/H/C/000082/SDA/040, MYCLAUSEN (CAP), MYCOPHENOLATE MOFETIL TEVA (CAP), MYFENAX (CAP), NAP

Applicant(s): Passauer Pharma GmbH (Myclausen), Roche Registration GmbH (Cellcept), Teva B.V. (Mycophenolate Mofetil Teva, Myfenax)

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of posterior reversible encephalopathy syndrome (PRES)

Action: For adoption of PRAC recommendation

EPITT 19473 – Follow-up to November 2019

4.3.5. Paroxetine (NAP)

Applicant(s): various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of microscopic colitis

Action: For adoption of PRAC recommendation

EPITT 19474 – Follow-up to November 2019

4.3.6. Thiazide, thiazide-like diuretics and combinations: bendroflumethiazide (NAP); chlortalidone (NAP); cicletanine (NAP); clopamide (NAP); cyclopenthiazide (NAP); hydrochlorothiazide (NAP); hydrochlorothiazide, aliskiren – RASILEZ HCT (CAP); hydrochlorothiazide, amlodipine, valsartan - EXFORGE HCT (CAP); hydrochlorothiazide, irbesartan – COAPROVEL (CAP), IFIRMACOMBI (CAP), IRBESARTAN HYDROCHLOROTHIAZIDE ZENTIVA (CAP), IRBESARTAN/HYDROCHLOROTHIAZIDE TEVA (CAP), KARVEZIDE (CAP); hydrochlorothiazide, telmisartan – ACTELSAR HCT (CAP), KINZALKOMB (CAP), MICARDISPLUS (CAP), PRITORPLUS (CAP), TOLUCOMBI (CAP); hydrochlorothiazide, valsartan, amlodipine - COPALIA HCT (CAP), DAFIRO HCT (CAP);

hydroflumethiazide (NAP); indapamide (NAP); metipamide (NAP); metolazone (NAP); xipamide (NAP)

Applicant(s): Actavis group PTC ehf (Actelsar HCT), Bayer AG (Kinzalkomb, PritorPlus), Boehringer Ingelheim International GmbH (MicardisPlus), Krka, d.d., Novo mesto (Ifirmacombi, Tolucombi), Noden Pharma DAC (Rasilez HCT), Novartis Europharm Limited (Copalia HCT, Dafiro HCT, Exforge HCT), Sanofi-Aventis groupe (CoAprovel, Karvezide), Teva B.V. (Irbesartan/Hydrochlorothiazide Teva), Zentiva k.s. (Irbesartan Hydrochlorothiazide Zentiva), various

PRAC Rapporteur: Martin Huber

Scope: Signal of choroidal effusion

Action: For adoption of PRAC recommendation

EPITT 19468 – Follow-up to December 2019

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Apixaban - EMEA/H/C/005358

Scope: Prevention of venous thromboembolic events (VTE), prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF), treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE

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

5.1.2. Aripiprazole - EMEA/H/C/005062

Scope: Treatment of schizophrenia, moderate to severe manic episodes in bipolar I disorder with sensor to measure medication adherence

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

5.1.3. Autologous CD34^{+} cell enriched population that contains hematopoietic stem and progenitor cells transduced ex vivo using a lentiviral vector encoding the human arylsulfatase A gene - EMEA/H/C/005321, Orphan

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP[6]

Scope (accelerated assessment): Treatment of metachromatic leukodystrophy (MLD)

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

[6] Advanced therapy medicinal product

5.1.4. Doxorubicin - EMEA/H/C/005320

Scope: Treatment of breast cancer, ovarian cancer, progressive multiple myeloma and acquired immune deficiency syndrome (AIDS)-related Kaposi's sarcoma

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

5.1.5. Fenfluramine - EMEA/H/C/003933, Orphan

Applicant: Zogenix GmbH

Scope: Treatment of seizures associated with Dravet syndrome in children aged 2 years to 17 years and adults

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

5.1.6. Indacaterol, mometasone furoate - EMEA/H/C/005516

Scope: Treatment of asthma

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

5.1.7. Lefamulin - EMEA/H/C/005048

Scope: Treatment of community-acquired pneumonia (CAP)

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

5.1.8. Melphalan - EMEA/H/C/005173

Scope: Treatment of multiple myeloma, malignant lymphoma (Hodgkin, non-Hodgkin lymphoma), acute lymphoblastic and myeloblastic leukaemia, childhood neuroblastoma, ovarian adenocarcinoma and mammary adenocarcinoma as well as conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (HSCT) in haematological diseases

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

5.1.9. Methylthioninium chloride - EMEA/H/C/002776

Scope: Aid for the enhanced visualisation and detection of colorectal lesions in adult patients undergoing screening/surveillance colonoscopy for colorectal cancer

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

5.1.10. Obiltoxaximab - EMEA/H/C/005169, Orphan

Applicant: SFL Regulatory Services GmbH

Scope: Treatment of inhalational anthrax due to Bacillus anthracis

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

5.1.11. Trastuzumab- EMEA/H/C/005209

Scope: Treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

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. 5-aminolevulinic acid - AMELUZ (CAP) - EMEA/H/C/002204/II/0040

Applicant: Biofrontera Bioscience GmbH

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 11.1) brought in line with revision 2 of GVP module V on 'Risk management systems', including also the implementation of changes as requested by PRAC in the conclusions of the periodic safety update report single assessment (PSUSA) procedure PSUSA/00010006/201806 adopted in February 2019

Action: For adoption of PRAC Assessment Report

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

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Adrien Inoubli

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

Action: For adoption of PRAC Assessment Report

5.2.3. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0033, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Submission of an updated RMP (version 11) in line with revision 2 of GVP module V on 'Risk management systems'. The protocol for study 20150136 (listed as a category 1 in the RMP/Annex II): an observational study of blinatumomab safety and effectiveness, utilisation, and treatment practices is updated and the enrolment period extended by 1 year. As a consequence, the milestones in the RMP are updated accordingly. In addition, the RMP includes a proposed update to the milestone of study 20180138 (listed as a category 3 study in the RMP): long-term follow-up of patients enrolled in TOWER study (a phase 3, randomized, open label study investigating the efficacy of the bispecific T-cell engager (BiTE) antibody blinatumomab versus standard of care chemotherapy in adult subjects with relapsed/refractory B-precursor acute lymphoblastic leukaemia (ALL))

Action: For adoption of PRAC Assessment Report

5.2.4. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/II/0015, Orphan

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 9.0) in order to remove as missing information drug-drug interaction, use in adolescents, adults and elderly, use in patients with an ethnic origin other than Caucasian, use in patients with hepatic and renal impairment as well as potential harm from overdose

Action: For adoption of PRAC Assessment Report

5.2.5. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/II/0052

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of an updated RMP (version 19.2) in order to update information relating to educational material to include greater emphasis on off label use and the risk of misuse and abuse. In addition, the MAH submitted a synopsis of a protocol for a PASS (as a category 3 study in the RMP) to assess the impact of the updated educational material

Action: For adoption of PRAC Assessment Report

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

Applicant: Merck Europe B.V.

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC Assessment Report

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

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 5.3) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template), to remove the important identified risks of 'ovarian hyperstimulation syndrome (OHSS)', 'thromboembolic events

usually with OHSS' and 'hypersensitivity reactions', to remove the important potential risks of 'breast cancer', 'ovarian cancer', 'endometrial cancer', 'congenital anomalies' and 'malignant melanoma'

Action: For adoption of PRAC Assessment Report

5.2.8. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/II/0081

Applicant: BioMarin International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 6.0) in order to update the safety specifications based on a review of the preclinical, clinical, post-marketing and literature data. In addition, the MAH took the opportunity to update the RMP in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.9. Human coagulation factor VIII, human von Willebrand factor - VONCENTO (CAP) - EMEA/H/C/002493/II/0042

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 7) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and reflect the completion of study CSLCT-BIO-12-83: a post-marketing study (PMS) to collect long-term data on the haemostatic efficacy of human coagulation factor VIII/von Willebrand factor (FVIII/VWF) complex in patients with von Willebrand Disease (VWD) who require a VWF product to control a bleeding event or as prophylaxis therapy. In addition, the RMP is updated to request a waiver to study Biostate_4001 (listed as a category 3 study in the RMP): a low-interventional multicentre PASS for Vocento (FVIII/VWF) for routine prophylaxis, treatment of bleeding events and/or surgery in male patients with haemophilia A due to feasibility reasons

Action: For adoption of PRAC Assessment Report

5.2.10. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/II/0052

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP to replace the prospective observational cohort study of Flixabi in patients with Crohn's disease (CD) (SB2-G42-CD), with real-world data from the following studies: 1) PERFUSE: a French cohort study with the primary aim to evaluate the persistence of Flixabi (infliximab) treatment over one year; 2) CREDIT: a nationwide German inflammatory bowel disease (IBD) registry: a long term observation of IBD patients; 3) CEDUR: Czech register of IBD patients on biological therapy

Action: For adoption of PRAC Assessment Report

5.2.11. Lonoctocog alfa - AFSTYLA (CAP) - EMEA/H/C/004075/II/0030

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Submission of an updated RMP (version 5.0) to introduce information on ongoing study CSL627_3001: a phase 3 open label, multicentre, extension study to assess the safety and efficacy of recombinant coagulation factor VIII (rVIII-single-chain CSL627 (lonoctocog alfa)) in subjects with severe haemophilia A. The RMP is also amended to reflect updated information on registries/non-interventional study (NIS) to demonstrate how previously untreated patient (PUP) clinical data will be complemented following the stop of enrolment of arm 2 of study CSL627 3001. The registries (e.g. addition of registry American Thrombosis and Hemostasis Network [ATHN] 8, removal of registries ATHN 2 and Dutch haemophilia registry) considered as additional pharmacovigilance activities have been updated respectively

Action: For adoption of PRAC Assessment Report

5.2.12. Lopinavir, ritonavir - ALUVIA (Art 58[7]) - EMEA/H/W/000764/WS1711/0112;KALETRA (CAP) - EMEA/H/C/000368/WS1711/0181

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of an updated RMP (version 9.0) in order to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template). The MAH took the opportunity to review the safety information contained in the RMP, removed an important potential risk of drug interaction with telaprevir and boceprevir (hepatitis C virus (HCV) protease inhibitors) and missing information regarding use of lopinavir/ritonavir (LPV/r) in elderly patients

Action: For adoption of PRAC Assessment Report

5.2.13. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/II/0053, Orphan

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Annika Folin

Scope: Submission of an updated RMP (version 20) in order to remove study AP24534-14-401: a post-marketing observational registry to evaluate the incidence of and risk factors for vascular occlusive events associated with Iclusig (ponatinib) in routine clinical practice in the US (OMNI) from the pharmacovigilance plan. In addition, the MAH took the opportunity to remove the distribution of the educational material in line with the conclusions of variation II/51 adopted in September 2019

Action: For adoption of PRAC Assessment Report

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

5.2.14. Telotristat ethyl - XERMELO (CAP) - EMEA/H/C/003937/II/0021, Orphan

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of an updated RMP (version 5.0) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

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

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

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Hans Christian Siersted

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

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

5.3.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0033

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumours express programmed death-ligand 1 (PD-L1) based on the results of pivotal study GO29431 (IMpower110): a phase 3, open label, randomized study of atezolizumab compared with a platinum agent (cisplatin or carboplatin) in combination with either pemetrexed or gemcitabine for PD-L1-selected, chemotherapy-naive patients with stage IV non-squamous or squamous NSCLC. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 12.0) are updated accordingly

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

5.3.3. Autologous CD34^{+} enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ANA cDNA sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/II/0024, Orphan

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP[8]

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information following the completion of study STRIM-004 (listed as a category 3 study in the

[8] Advanced therapy medicinal product

RMP): a non-interventional long term follow up of the subjects including paediatric patients who received Strimvelis gene therapy. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor administrative changes in the product information

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

5.3.4. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0016

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include a new indication in the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 8.1) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to introduce minor editorial changes to the labelling. Furthermore, Annex II is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.5. Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - TRIMBOW (CAP) - EMEA/H/C/004257/X/0008/G

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Grouped application consisting of: 1) extension application to introduce a new strength (172 µg / 5 µg / 9 µg); 2) update of sections 4.1, 4.2, 4.4, 5.1 and 5.2 to extend the indication to the maintenance treatment in adult patients with asthma who are not adequately treated by a combination of an inhaled corticosteroid and a long-acting beta2-agonist or who are already treated by a combination of an inhaled corticosteroid and a long-acting beta2-agonist plus a long-acting muscarinic antagonist. The RMP (version 6.1) is updated in accordance

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

5.3.6. Bortezomib - BORTEZOMIB FRESENIUS KABI (CAP) - EMEA/H/C/005074/II/0001/G

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Grouped variations consisting of: 1) addition of a new pack size for the solution for injection, with a fill volume for a single dose vial of 1 mg per vial in addition to the authorised 3.5 mg per vial; 2) addition of a new pack size for the powder for solution for injection with a fill volume for a single dose vial of 2.5 mg per vial in addition to the authorised 3.5 mg per vial. The RMP (version 2.0) is updated accordingly

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

5.3.7. Budesonide - JORVEZA (CAP) - EMEA/H/C/004655/X/0007/G, Orphan

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Grouped application consisting of: 1) extension application to add a new strength of 0.5 mg for budesonide orodispersible tablets; 2) extension of indication to include the maintenance of remission for the 0.5 mg and 1 mg orodispersible tablets. As a consequence, sections 4.2, 4.8 and 5.1 of the SmPC are updated to reflect the recommended daily dose and duration of treatment of Jorveza (budesonide) for the maintenance of remission, to update the list of adverse reactions and the clinical efficacy and safety information based on the results of study BUL-2/EER: a double-blind, randomized, placebo-controlled, phase 3 study on the efficacy and tolerability of a 48-week treatment with two different doses of budesonide effervescent tablets vs. placebo for maintenance of clinico-pathological remission in adult patients with eosinophilic esophagitis. The package leaflet is updated accordingly. In addition, the RMP (version 2.0) is updated accordingly and is brought in line with revision 2 of the guidance on the format of RMP in the EU (template). The MAH also took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1); 3) addition of a new pack-size of 200 x 1 orodispersible tablets (unit dose) in a blister for Jorveza (budesonide) 1 mg orodispersible tablet

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

5.3.8. Ceftazidime, avibactam - ZAVICEFTA (CAP) - EMEA/H/C/004027/II/0015

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to include paediatric patients aged 3 months to less than 18 years for Zavicefta (ceftazidime/avibactam) based on data from three paediatric studies namely, study D4280C00014: a phase 1 study to assess the pharmacokinetics, safety and tolerability of a single dose of ceftazidime-avibactam (CAZ-AVI) in children from 3 months of age to <18 years who are receiving systemic antibiotic therapy for suspected or confirmed infection; study C3591004: a single blind, randomised, multicentre, active controlled, trial to evaluate safety, tolerability, pharmacokinetics (PK) and efficacy of ceftazidime and avibactam when given in combination with metronidazole, compared with meropenem, in children from 3 months to less than 18 years of age with complicated intra-abdominal infections (cIAIs); and study C3591005: a single blind, randomised, multicentre, active controlled, trial to evaluate safety, tolerability, pharmacokinetics and efficacy of ceftazidime and avibactam compared with cefepime in children from 3 months to less than 18 years of age with complicated urinary tract infections (CUTIs); as well as population PK modelling/simulation analyses (CAZ-MS-PED-01 and CAZ-MS-PED-02). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.3 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to correct sections 2 and 4.4 of the SmPC and the package leaflet with information on sodium content, as well as section 5.2 of the SmPC with information on volumes of distribution of ceftazidime and avibactam. Furthermore, the MAH also introduced minor correction in the Czech product information

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

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

Applicant: Pharming Group N.V

PRAC Rapporteur: Jan Neuhauser

Scope: Grouped variations consisting of an extension of indication to include children in the treatment of acute angioedema attacks with hereditary angioedema (HAE) due to C1 esterase inhibitor deficiency, based on the results from study C1 1209: an open-label, phase 2, single arm study to evaluate the safety, immunogenicity, pharmacokinetics and efficacy of recombinant human C1 inhibitor for the treatment of acute attacks in paediatric patients with hereditary angioedema, from 2 up to and including 13 years of age. In addition, final efficacy and safety data from the open label extension (OLE) phases of 1) study C1 1304: a randomised, placebo-controlled, double-blind, multicentre study performed in order to demonstrate the efficacy of recombinant human C1 inhibitor (rhC1INH) at 100 U/kg in patients with HAE with attacks of angioedema; 2) study C1 1205: a randomised, placebo-controlled, double-blind phase 2 study on the safety and efficacy of rhC1INH at doses of 50 and 100U/kg in relieving eligible attacks of angioedema with involvement of sub-mucosal tissues in patients with HAE; and completed study C1 1310: a phase 3, randomized, placebo-controlled trial on rhC1INH relieved symptoms of hereditary angioedema attacks; together with the final results of studies C1 1207 and 3201 concerning prophylactic treatment of HAE patients. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.7, 4.8, 5.1, 5.2 and 5.3 are updated. The package leaflet and the RMP (version 19.0) are updated accordingly. The RMP is also brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). Furthermore, the MAH requested an extension for the completion of registry study C1 1412: C1 inhibitor treatment registry to assess the safety and immunological profile of Ruconest (conestat alfa) in the treatment of HAE attacks, from March 2020 to June 2022. Finally, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.10. Desloratadine - DESLORATADINE RATIOPHARM (CAP) - EMEA/H/C/002404/II/0023/G

Applicant: ratiopharm GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Grouped variations consisting of: 1) change in the legal status of Desloratadine ratiopharm from 'medicinal product subject to medical prescription' to 'medicinal product not subject to medical prescription' in view of the safety profile of Desloratadine ratiopharm and the post-marketing experience already available with other medicinal products containing similar long acting histamine antagonists. The RMP (version 1.0) is updated accordingly. In addition, the MAH also took the opportunity to bring the product information (PI) in line with the latest quality review of documents (QRD) template (version 10.1), to update the list of local representatives in the package leaflet and to introduce editorial changes.; 2) deletion of the therapeutic indication in adolescents aged 12 years and older for the relief of symptoms associated with allergic rhinitis and urticaria. As a consequence, section 4.1 of the SmPC is updated. The package leaflet is updated accordingly

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

5.3.11. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/X/0045

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Extension application to introduce two new strengths of 3 mg and 4.5 mg solution for injection. The RMP (version 4.1) is updated accordingly

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

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

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Adrien Inoubli

Scope: Extension of indication in order to include patient population from 2 to 6 years of age based on the 48 week study results from study TMC125-C234/P1090: a phase 1/2, open-label trial to evaluate the safety, tolerability, pharmacokinetics and antiviral activity of etravirine (ETR) in antiretroviral (ARV) treatment-experienced human immunodeficiency virus-1 (HIV-1) infected infants and children, aged ≥2 months to <6 years. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 13.1) are updated accordingly. The RMP is also brought in line with revision 2 of GVP module V on 'Risk management systems' and revision 2.0.1 of the guidance on the format of RMP in the EU (template) leading to a reclassification of safety concerns. Finally, the MAH took the opportunity to introduce minor updates to the product information

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

5.3.13. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0020

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4 and 4.8 of the SmPC to include anaphylactic reactions as an adverse drug reaction. The package leaflet and the RMP (version 5.2) are updated accordingly

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

5.3.14. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - CERVARIX (CAP) - EMEA/H/C/000721/II/0106

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.4 and 5.1 of the SmPC based on final results from study HPV-019 (listed as a category 3 study in the RMP) (in fulfilment of MEA 080): a safety and immunogenicity study of Cervarix (human papillomavirus vaccine) in human immunodeficiency virus (HIV)-positive female subjects aged 15-25 years as compared to human papillomavirus 4 (HPV-4). In addition, the MAH took the opportunity to reflect an

update in section 4.2 of the SmPC to indicate that limited clinical data is now available in 4-6 years old children based on study HPV-073: a safety and immunogenicity study of Cervarix (human papillomavirus vaccine) in girls aged 4-6 years, as an alternative to the current adolescent HPV vaccination schedule. The RMP (version 21.0) is updated accordingly and also reflect the removal of the use of Cervarix (human papillomavirus vaccine) in HIV-infected subjects or subjects with known immune deficiencies as missing information. Furthermore, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

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

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Ilaria Baldelli

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

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

5.3.16. Iron - VELPHORO (CAP) - EMEA/H/C/002705/II/0021

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 5.1 of the SmPC in order to add information related to the results of the VERIFIE study (listed as a category 3 study in the RMP): a non-interventional voluntary PASS trial to investigate the short and long-term real-life safety, effectiveness, and adherence of Velphoro (iron) in patients with hyperphosphataemia undergoing haemodialysis or peritoneal dialysis. Furthermore, minor editorial changes in section 4.2 of the SmPC were introduced to provide consistent information between the SmPC, the labelling and the package leaflet. The RMP (version 8.0) is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.17. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/X/0083/G, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped variations consisting of: 1) extension application to add a new strength of 75 mg film-coated tablets of ivacaftor to enable administration to patients aged 6 to less than 11 years; 2) update of sections 4.1, 4.2 and 6.5 the SmPC for the 150 mg film-coated tablet presentations to extend the indication for use in children aged 6 to less than 11 years old in combination with tezacaftor/ivacaftor and to bring it in line with the new dosage form.

The package leaflet and the RMP (version 8.6) are updated in accordance. In addition, the MAH took the opportunity to implement minor updates throughout the product information

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

5.3.18. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0019/G, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of: 1) submission of the final report from study NSMM-5001 (listed as a specific obligation (SOB) in Annex II-E on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation): a global, prospective, non-interventional, observational efficacy study in multiple myeloma patients. Annex II and the RMP (version 5) are updated accordingly; 2) submission of an updated RMP (version 5) in order to extend the due date of post-authorisation efficacy study (PAES) C16010 (listed in Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product': provision of an interim report of overall survival (OS) at the time of the third interim analysis and provision of a final report for the final analysis of OS from the phase 3, randomized, double-blind study C16010 in adult patients with relapsed and/or refractory multiple myeloma. The MAH took the opportunity to correct a typographical error in Annex II

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

5.3.19. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/II/0030

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with active axial spondyloarthritis. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 10.1) are updated accordingly. The product information is also brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.20. Lacosamide - LACOSAMIDE ACCORD (CAP) - EMEA/H/C/004443/X/0007

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to introduce a new pharmaceutical form (solution for infusion), a new strength (10mg/ml) and a new route of administration (intravenous use). The RMP (version 1.0) is updated accordingly

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

5.3.21. Lidocaine, prilocaine - FORTACIN (CAP) - EMEA/H/C/002693/II/0030

Applicant: Recordati Ireland Ltd

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Change in the legal status from 'medicinal product subject to medical prescription' to 'medicinal product not subject to medical prescription' in view of the safety profile of Fortacin (lidocaine/prilocaine), the post-marketing experience already available with other medicinal products containing amide local anaesthetics and in view of making the medicinal product more accessible to the target population. The RMP (version 3.1) is updated accordingly. Furthermore, the product information is also brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.22. Lurasidone - LATUDA (CAP) - EMEA/H/C/002713/II/0029

Applicant: Aziende Chimiche Riunite Angelini Francesco S.p.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to add the treatment of schizophrenia in adolescent from 13 to less than 18 years. As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The package leaflet and the RMP (version 8.0) are updated accordingly. In addition, the MAH took the opportunity to update the product information in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' 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

5.3.23. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/II/0023

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and immunogenicity information based on final results from study B1971033 (listed as a category 3 study in the RMP) (in fulfilment of MEA 007): a duration of immunity study to assess persistence of hSBA (serum bactericidal activity using human complement) response for up to 48 months after completion of vaccination with Trumenba (meningococcal group B vaccine) and the immunogenicity, safety, and tolerability of a booster dose of Trumenba (meningococcal group B vaccine). The RMP (version 3) is updated accordingly and includes changes agreed in variation II/13 as well as editorial changes. In addition, the MAH took the opportunity to introduce editorial changes in Annex II, in the labelling and in the package leaflet

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

5.3.24. Meningococcal group B vaccine (recombinant, component, adsorbed) - BEXSERO (CAP) - EMEA/H/C/002333/II/0088

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to reflect the final results from study V72_38OB (listed as category 3 study in the RMP): an observational effectiveness study of the impact of Bexsero (meningococcal group B vaccine) vaccination. The package leaflet and the RMP (version 7.3) are updated accordingly. In addition, the MAH took the opportunity to introduce some rewording in section 5.1 of the SmPC, to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1) and to amend minor typos detected in the European annexes

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

5.3.25. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/II/0027, Orphan

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype based on the results of pharmacology studies and the double-blind, randomised, placebo-controlled phase 3 trial (INBUILD). 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 formatting changes in the product information. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.26. Nomegestrol acetate, estradiol - ZOELY (CAP) - EMEA/H/C/001213/II/0050

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Adrien Inoubli

Scope: Update of sections 4.3 and 4.4 of the SmPC in order to add a new contraindication and a new warning regarding meningioma, as requested in the conclusions of LEG 014 finalised in March 2019. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Netherlands and Portugal in the package leaflet

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

5.3.27. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0035

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include the use of Lynparza (olaparib) tablets in

combination with bevacizumab for the maintenance treatment of adult patients with advanced (FIGO[9] stages III and IV) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy with bevacizumab. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC are updated. The package leaflet and the RMP (version 19.0) are updated accordingly. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza (olaparib) hard capsules are revised based on updated safety data analysis. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.28. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0036

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include the use of Lynparza (olaparib) tablets as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and homologous recombination repair gene mutations (germline and/or somatic) who have progressed following a prior new hormonal agent. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 20) are updated accordingly. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza (olaparib) hard capsules are revised based on updated safety data analysis

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

5.3.29. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - SYNFLORIX (CAP) - EMEA/H/C/000973/II/0146

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from a hospital-based surveillance study assessing the impact of Synflorix (pneumococcal polysaccharide conjugate vaccine) immunisation programme in Kenya on pneumonia, invasive pneumococcal disease (IPD) and replacement disease (in fulfilment of post-authorisation measure MEA 021.8). The RMP (version 18) is updated accordingly. In addition, the RMP is updated in line with revision 2 of GVP module V on 'Risk management systems'

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

5.3.30. Ramucirumab - CYRAMZA (CAP) - EMEA/H/C/002829/II/0038

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add posterior reversible encephalopathy syndrome (PRES) and dysphonia as a warning and as an undesirable effect

[9] International Federation of Gynaecology and Obstetrics

respectively. The labelling, package leaflet and the RMP (version 9.3) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.31. Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/II/0002

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include the treatment of patients with atypical haemolytic uremic syndrome (aHUS). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 1.6) are updated accordingly. In addition, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated to include in the educational materials the risk of thrombotic microangiopathy (TMA) with the new indication

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

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

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Hans Christian Siersted

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

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

5.3.33. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0044

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Update of the SmPC sections 5.1 and 4.8 with efficacy and safety information to reflect the 5-year follow-up data from the final clinical study report (CSR) of study B2301 week 256 (as an imposed study in Annex II-D 'Conditions or restrictions with regard to the safe and effective use of the medicinal product'): a phase 3, open-label, randomised, controlled study comparing the efficacy and safety of the JAK inhibitor ruxolitinib to best available therapy (BAT) in adult patients with polycythemia vera (PV) who were resistant to or intolerant of hydroxyurea. The RMP (version 11) is updated accordingly (assessed with variation II/43)

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

5.3.34. Sebelipase alfa - KANUMA (CAP) - EMEA/H/C/004004/II/0026/G, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the clinical information based on the pooled safety and efficacy analysis of already submitted studies (namely study LAL-CL04: an open label multicentre extension study to evaluate the long-term safety, tolerability, and efficacy of sebelipase alfa (SBC-102) in adult subjects with liver dysfunction due to lysosomal acid lipase deficiency (LAL-D) who previously received treatment in study LAL-CL01; study LAL-CL03: an open label, multicentre, dose escalation study to evaluate the safety, tolerability, efficacy, pharmacokinetics, and pharmacodynamics of SBC-102 in children with growth failure due to LAL-D; study LAL-CL06: a multicentre, open-label study of sebelipase alfa in patients with LAL-D; study LAL-CL08: a phase 2, open label, multicentre study to evaluate the safety, tolerability, efficacy, and pharmacokinetics of sebelipase alfa in infants with rapidly progressive LAL-D; study LAL-CL02: a multicentre, randomized, placebo-controlled study of SBC-102 in patients with LAL-D) and updated population pharmacokinetic (PK) analyses in children and adults. The package leaflet and the RMP (version 4.0) are updated accordingly. Annex II is also updated to remove the obligation related to the provision of study LAL-CL08; 2) submission of the final report from study LAL-EA01: an open-label study with sebelipase alfa 1 mg/kg every other week for up to 78 weeks or until drug commercialisation in the United States (US) patients who did not otherwise qualify for an active sebelipase alfa trial (expanded access protocol)

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

5.3.35. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0053/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) extension of indication to include the treatment of non-radiographic axial spondyloarthritis (nr-axSpA)/axial spondyloarthritis (axSpA) without radiographic evidence. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 of the SmPC are amended. The package leaflet and the RMP (version 5.0) are updated accordingly; 2) change in the due date of the psoriasis registry (listed as a category 3 study in the RMP)

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

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

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Željana Margan Koletić

Scope: Submission of the final report of study CLDE225X2116 (listed as a category 3 study in the RMP): an interventional phase 1b/2, open-label, multicentre, dose-finding study to

assess the safety and efficacy of the oral combination of LDE225 (sonidegib) and INC424 (ruxolitinib) in subjects with myelofibrosis. The RMP (version 7.1) is updated accordingly

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

5.3.37. Talazoparib - TALZENNA (CAP) - EMEA/H/C/004674/II/0001

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in patients with severe renal impairment and update pharmacokinetic (PK) information based on the results from PK study MDV3800-01 (C3441001) (listed as a category 3 study in the RMP): a phase 1 open-label pharmacokinetics and safety study of talazoparib (MDV3800) in patients with advanced solid tumours and normal or varying degrees of renal impairment. The RMP (version 1.0) is updated accordingly. In addition, the MAH took the opportunity to introduce minor changes throughout the product information and to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.38. Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/X/0015/G, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped variations consisting of: 1) extension application to add a new strength of 50/75mg film-coated tablets of tezacaftor/ivacaftor to enable administration to patients aged 6 to less than 11 years; 2) update of sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.1 of the SmPC for the 100/150 mg film-coated tablet presentations to extend the indication for use in children aged 6 to less than 11 years old in combination with ivacaftor and to bring it in line with the new dosage form. The package leaflet and the RMP (version 2.1) are updated in accordance. In addition, the MAH took the opportunity to implement minor updates in the product information

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

5.3.39. Thiotepa - TEPADINA (CAP) - EMEA/H/C/001046/X/0036, Orphan

Applicant: Adienne S.r.l.

PRAC Rapporteur: Ghania Chamouni

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (400 mg powder and solvent for solution for infusion). The RMP (version 14) is updated accordingly

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

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

Applicant: Mylan S.A.S

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Agalsidase beta - FABRAZYME (CAP) - PSUSA/00000070/201907

Applicant: Genzyme Europe BV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - ZALMOXIS[10] - PSUSA/00010530/201908

Applicant: MolMed S.p.A, ATMP[11]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of PRAC Rapporteur assessment report

6.1.3. Asenapine - SYCREST (CAP) - PSUSA/00000256/201908

Applicant: N.V. Organon

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[10] European Commission (EC) marketing authorisation withdrawal dated 09 October 2019
[11] Advanced therapy medicinal product

6.1.4. Baricitinib - OLUMIANT (CAP) - PSUSA/00010578/201908

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Burosumab - CRYSVITA (CAP) - PSUSA/00010669/201908

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Caplacizumab - CABLIVI (CAP) - PSUSA/00010713/201908

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Chlormethine - LEDAGA (CAP) - PSUSA/00010587/201908

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Cobicistat - TYBOST (CAP) - PSUSA/00010081/201908

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Cobicistat, elvitegravir, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - PSUSA/00010082/201908

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Cobimetinib - COTELLIC (CAP) - PSUSA/00010450/201908

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Copper (^{64}Cu) chloride - CUPRYMINA (CAP) - PSUSA/00010040/201908

Applicant: A.C.O.M. - Advanced Center Oncology

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Dabrafenib - TAFINLAR (CAP) - PSUSA/00010084/201908

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Damoctocog alfa pegol - JIVI (CAP) - PSUSA/00010732/201908

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Doravirine - PIFELTRO (CAP) - PSUSA/00010729/201908

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Doravirine, lamivudine, tenofovir disoproxil - DELSTRIGO (CAP) - PSUSA/00010731/201908

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Dronedarone - MULTAQ (CAP) - PSUSA/00001180/201907

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Eliglustat - CERDELGA (CAP) - PSUSA/00010351/201908

Applicant: Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Eravacycline - XERAVA (CAP) - PSUSA/00010718/201908

Applicant: Tetraphase Pharmaceuticals Ireland Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/201908

Applicant: Chiesi Farmaceutici S.p.A., ATMP[12]

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.20. Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/201908

Applicant: Norgine B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Advanced therapy medicinal product

6.1.21. Human alpha$_1$-proteinase inhibitor[13] - RESPREEZA (CAP) - PSUSA/00010410/201908

Applicant: CSL Behring GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Hydrocortisone[14] - ALKINDI (CAP) - PSUSA/00010674/201908

Applicant: Diurnal Europe BV

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Influenza vaccine (intranasal, live attenuated) - FLUENZ TETRA (CAP) - PSUSA/00001742/201908

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Lanadelumab - TAKHZYRO (CAP) - PSUSA/00010743/201908

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Linaclotide - CONSTELLA (CAP) - PSUSA/00010025/201908

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Mecasermin - INCRELEX (CAP) - PSUSA/00001942/201908

Applicant: Ipsen Pharma

[13] Centrally authorised product(s) only
[14] Centrally authorised product(s) only, indicated for adrenal insufficiency, paediatric use only

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Meropenem, vaborbactam - VABOREM (CAP) - PSUSA/00010727/201908

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Nonacog alfa - BENEFIX (CAP) - PSUSA/00002183/201908

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Pandemic influenza vaccine (H5N1) (whole virion, Vero cell derived, inactivated) - PANDEMIC INFLUENZA VACCINE H5N1 BAXTER (CAP); prepandemic influenza vaccine (H5N1) (whole virion, Vero cell derived, inactivated) - VEPACEL (CAP) - PSUSA/00002282/201908

Applicant: Ology Bioservices Ireland Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Panobinostat - FARYDAK (CAP) - PSUSA/00010409/201908

Applicant: Secura Bio Limited

PRAC Rapporteur: Sofia Trantza

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Patisiran - ONPATTRO (CAP) - PSUSA/00010715/201908

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Peginterferon alfa-2b - PEGINTRON (CAP); VIRAFERONPEG (CAP) - PSUSA/00002327/201907

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Pembrolizumab - KEYTRUDA (CAP) - PSUSA/00010403/201909

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Pyronaridine, artesunate - PYRAMAX (Art 58[15]) - EMEA/H/W/002319/PSUV/0021

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.35. Rolapitant - VARUBY (CAP) - PSUSA/00010592/201908

Applicant: Tesaro Bio Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Romiplostim - NPLATE (CAP) - PSUSA/00002660/201907

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Ropeginterferon alfa-2b - BESREMI (CAP) - PSUSA/00010756/201908

Applicant: AOP Orphan Pharmaceuticals AG

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

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Sebelipase alfa - KANUMA (CAP) - PSUSA/00010422/201908

Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Teduglutide - REVESTIVE (CAP) - PSUSA/00009305/201908

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Telotristat - XERMELO (CAP) - PSUSA/00010639/201908

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Tezacaftor, ivacaftor - SYMKEVI (CAP) - PSUSA/00010730/201908

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Tisagenlecleucel - KYMRIAH (CAP) - PSUSA/00010702/201908

Applicant: Novartis Europharm Limited, ATMP[16]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

[16] Advanced therapy medicinal product

6.1.43. Tivozanib - FOTIVDA (CAP) - PSUSA/00010636/201908

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Vemurafenib - ZELBORAF (CAP) - PSUSA/00009329/201908

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Palonosetron - ALOXI (CAP); NAP - PSUSA/00002268/201907

Applicant(s): Helsinn Birex Pharmaceuticals Limited (Aloxi), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Beclometasone, formoterol[17] (NAP) - PSUSA/00010068/201907

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Brivudine (NAP) - PSUSA/00000434/201907

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

[17] For inhalation use only

Action: For adoption of recommendation to CMDh

6.3.3. Busulfan (NAP) - PSUSA/00000464/201907

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Fosfomycin[18] (NAP) - PSUSA/00010336/201907

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Fosfomycin[19] (NAP) - PSUSA/00010326/201907

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Human coagulation factor IX (NAP) - PSUSA/00001617/201907

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Meloxicam (NAP) - PSUSA/00010474/201907

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[18] Intravenous (IV) formulation only
[19] Oral formulation only

6.3.8. Phleum pratense[20] [21] [22] (NAP) - PSUSA/00010475/201907

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Poliovirus type 1, poliovirus type 3 (oral, live, attenuated) vaccine (NAP) - PSUSA/00010642/201907

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Ropinirole (NAP) - PSUSA/00002661/201907

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Zaleplon (NAP) - PSUSA/00003140/201907

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

None

[20] Allergen for therapy
[21] For oromucosal use only
[22] Medicinal product(s) authorised via mutually recognition procedure only

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[23]

7.1.1. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - EMEA/H/C/PSA/S/0049

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Amendment to a protocol previously agreed in July 2018 (PSP/S/0057.1) for a cerebrotendinous xanthomatosis registry: a long term non-interventional follow-up of safety and effectiveness of Chenodeoxycholic acid Leadiant (chenodeoxycholic acid)]

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

7.1.2. Cholic acid - KOLBAM (CAP) - EMEA/H/C/PSA/S/0048

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Agni Kapou

Scope: Amendment to a protocol previously agreed in September 2017 (PSA/S/0021): a prospective, observational, non-interventional, post-marketing, patient registry to collect data on routine clinical care in patients treated with Kolbam (cholic acid)

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

7.1.3. Valproate (NAP) - EMEA/H/N/PSP/J/0074.2

Applicant: Sanofi-Aventis Recherche & Développement (on behalf of a consortium)

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to PSP/J/0074.1 [protocol for an observational study to evaluate and identify the best practices for switching of valproate in clinical practice, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in November 2019[24]

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

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

7.2.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 075.9

Applicant: AbbVie Deutschland GmbH & Co. KG

[23] In accordance with Article 107n of Directive 2001/83/EC
[24] Meeting held 28-31 October 2019
[25] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Amendment to a previously agreed protocol in August 2012 (FUM 075) for study P11-282 (Humira Adult Ulcerative Colitis Registry): a long-term non-interventional registry 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

7.2.2. Botulinum toxin type A - NUCEIVA (CAP) - EMEA/H/C/004587/MEA 002

Applicant: Evolus Pharma Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Protocol (version 1.0) for study EV-010: a non-interventional post-authorisation safety study of Nuceiva (botulinum toxin type A) for the treatment of moderate-to-severe glabellar lines

Action: For adoption of advice to CHMP

7.2.3. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 002.1

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to MEA 002 [protocol for observational cohort study TV48125-MH-50037: a pregnancy registry assessing pregnancy outcomes in patients treated with Ajovy (fremanezumab)] as per the request for supplementary information (RSI) adopted in September 2019

Action: For adoption of advice to CHMP

7.2.4. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 003.1

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to MEA 003 [protocol for observational cohort study TV48125-MH-50038: a pregnancy database study assessing pregnancy outcomes in patients treated with Ajovy (fremanezumab)] as per the request for supplementary information (RSI) adopted in September 2019

Action: For adoption of advice to CHMP

7.2.5. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 005

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol for study TV48125-MH-50039: a long-term, prospective, phase 4, observational study to evaluate the safety, including cardiovascular safety, of fremanezumab in patients with migraine in routine clinical practice

Action: For adoption of advice to CHMP

7.2.6. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/MEA 009

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Protocol for study EPI-ZOSTER-030 VS (targeted safety study): a non-interventional/observational prospective cohort study to evaluate the safety of Shingrix (herpes zoster vaccine) in older adults (⩾ 50 year of age) in the United States [final clinical study report (CSR) expected in March 2025] (from initial opinion/marketing autorisation)

Action: For adoption of advice to CHMP

7.2.7. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/MEA 020

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Protocol for study EPI-ZOSTER-032 VS: a non-interventional/observational targeted safety study to evaluate the safety of Shingrix (herpes zoster vaccine) in the Medicare population (65 years old or older) in the United States [final clinical study report (CSR) expected in June 2027]

Action: For adoption of advice to CHMP

7.2.8. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 020

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Protocol for study CT-P13 4.8: an observational, prospective cohort study to evaluate the safety of Remsima (infliximab) subcutaneous in patients with rheumatoid arthritis (RA)

Action: For adoption of advice to CHMP

7.2.9. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/MEA 036.2

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Amendment to protocol previously agreed in November 2018 for study CA184557: extension of the Dutch melanoma treatment registry (DMTR) to include paediatric subjects and collect safety data to obtain additional safety information in paediatric patients, as per the conclusion of variation II/64 concluded in October 2019 to add an additional milestone

Action: For adoption of advice to CHMP

7.2.10. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 002.1

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002 [protocol for study PUMA-NER-6202: a randomised study to characterise the incidence and severity of diarrhoea in patients with early stage epidermal growth factor receptor 2 + (HER2+) breast cancer treated with neratinib and intensive loperamide prophylaxis versus neratinib and intensive loperamide prophylaxis plus a bile acid sequestrant in the first month of treatment [final study results expected in December 2021] as per the request for supplementary information (RSI) adopted in July 2019

Action: For adoption of advice to CHMP

7.2.11. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 003

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for study 165-501: a multicentre, prospective global observational study to evaluate the long term safety of subcutaneous injections of pegvaliase in patients with phenylketonuria [final clinical study report (CSR) expected in Q2 2030] (from opinion/initial marketing authorisation)

Action: For adoption of advice to CHMP

7.2.12. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 004

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for study 165-503: a multicentre, prospective, longitudinal, observational study evaluating immunologic, inflammatory and laboratory parameters associated with long term Palynziq (pegvaliase) treatment in patients with phenylketonuria (PKU) in the United States [final clinical study report (CSR) expected in Q2 2030] (from opinion/initial marketing authorisation)

Action: For adoption of advice to CHMP

7.2.13. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 005

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for study 165-504: a prospective global multicentre observational safety surveillance study to assess maternal, foetal and infant outcomes of exposure to Palynziq (pegvaliase) during pregnancy and breastfeeding [final clinical study report (CSR) expected in Q2 2030] (from opinion/initial marketing authorisation)

Action: For adoption of advice to CHMP

7.2.14. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 005.6

Applicant: Teva B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for study C38072-AS-50027(listed as category 3 study in the RMP): a long-term non-interventional study comparing the potential risk of malignancy in severe asthma patients treated with reslizumab and patients not treated with reslizumab using secondary administrative healthcare data [final clinical study report

Action: For adoption of advice to CHMP

7.2.15. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 001.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH' response to MEA 001 [protocol for study P19-633: a post-marketing registry-based prospective cohort study of long-term safety of risankizumab in real world setting in Denmark and Sweden [final study report due in December 2031]] as per the request for supplementary information (RSI) adopted in November 2019

Action: For adoption of advice to CHMP

7.2.16. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 002.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH' response to MEA 002 [protocol for study P16-751 on pregnancy exposures and outcomes in psoriasis patients treated with risankizumab: a cohort study utilising large healthcare databases with mother-baby linkage in the United States [final study report expected in Q3 2026] (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in November 2019

Action: For adoption of advice to CHMP

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

7.3.1. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/PSR/S/0024

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Results for an observational post-authorisation safety specialist cohort event monitoring study (SCEM) to monitor the safety and utilisation of Xarelto (rivaroxaban) initiated in secondary care for the prevention of atherothrombotic events in patients who have had acute coronary syndrome in England and Wales

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

Action: For adoption of a recommendation to CHMP

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

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

Applicant: Genzyme Europe BV

PRAC Rapporteur: Liana Gross-Martirosyan

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

Action: For adoption of PRAC Assessment Report

7.4.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0079

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final report from study ALGMYC07390: prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions to test the effectiveness of the approved Safety Information Packet (SIP) (in fulfilment of MEA 053)

Action: For adoption of PRAC Assessment Report

7.4.3. Anakinra - KINERET (CAP) - EMEA/H/C/000363/II/0073

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of the final report from study Sobi.ANAKIN-302 (listed as a category 3 study in the RMP): a non-interventional PASS to evaluate the long-term safety of Kineret (anakinra) in patients with systemic juvenile idiopathic arthritis. The RMP (version 5.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

Applicant: Bristol-Myers Squibb Pharma EEIG

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

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of PRAC Assessment Report

7.4.5. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS1742/0037; FORXIGA (CAP) - EMEA/H/C/002322/WS1742/0056; dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/WS1742/0043; XIGDUO (CAP) - EMEA/H/C/002672/WS1742/0054

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Update of section 4.4 of the SmPC based on the final results of a PASS (listed as a category 3 study in the RMPs): a meta-analysis across the following studies: 1) study D1690C00018: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled, phase 3 study with a 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg once daily in patients with type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD) and hypertension who exhibit inadequate glycaemic control on usual care; 2) study D1690C00019: A 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled phase 3 study with an 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg once daily in patients with T2DM and CVD, who exhibit inadequate glycaemic control on usual care; 3) study D1693C00001 (DECLARE): a multicentre, randomized, double-blind, placebo-controlled trial to evaluate the effect of dapagliflozin 10 mg once daily on the incidence of cardiovascular death, myocardial infarction or ischemic stroke in patients with T2DM, for analysis of lower limb amputation and relevant preceding adverse events. The package leaflets are updated accordingly. In addition, the MAH took the opportunity to implement a minor editorial change in the product information of Edistride (dapagliflozin). The RMPs (version 19 for Edistride/Forxiga (dapagliflozin) and version 12 for Ebymect/Xigduo (dapagliflozin/metformin) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0048

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of the final study report from study B010 (listed as a category 3 study in the RMP) investigating the utilisation of dulaglutide in European countries: a cross-sectional, multi-country and multi-source drug utilisation study using electronic health record

databases (in fulfilment of MEA 001). The RMP (version 5.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/II/0043

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study linaclotide utilisation study in selected European populations (listed as a category 3 study in the RMP): a drug utilisation study (DUS) to address the following safety concerns: potential for off-label use and abuse/excessive use; use in pregnancy and lactation and male patients as well as off-label use and use in males and in pregnant female patients

Action: For adoption of PRAC Assessment Report

7.4.8. Maraviroc - CELSENTRI (CAP) - EMEA/H/C/000811/II/0061

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study A4001067 (POEM) (listed as a category 3 study in the RMP): a non-interventional international, multicentre, prospective observational study of the safety of maraviroc used with optimised background therapy in treatment-experienced human immunodeficiency virus 1 (HIV-1) infected patients. The RMP (version 12.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.9. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/II/0030, Orphan

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final report for study 16657, EXPERT (EXPosurE Registry RiociguaT in patients with pulmonary hypertension) (listed as a category 3 study in the RMP) to collect information about the long term use of Adempas (riociguat) in real clinical practice. The RMP (version 7.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.10. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0043

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report for study INC424AIC01T (listed as a category 3 study in the RMP): a non-interventional, observational PASS in order to provide real-world safety data on patients with myelofibrosis (MF) who were exposed and non-exposed to ruxolitinib and provide insights into disease management and the safety profile of ruxolitinib. The RMP

(version 11.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.11. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0094

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study WA22480 ((listed as a category 3 study in the RMP): a phase 4, prospective observational cohort study using Sweden registers to provide long term safety data from the use of tocilizumab in Sweden for rheumatoid arthritis (RA) patients (ARTIS[28])

Action: For adoption of PRAC Assessment Report

7.4.12. Umeclidinium bromide - INCRUSE ELLIPTA (CAP) - EMEA/H/C/002809/WS1761/0028; ROLUFTA ELLIPTA (CAP) - EMEA/H/C/004654/WS1761/0013 Umeclidinium, vilanterol - ANORO ELLIPTA (CAP) - EMEA/H/C/002751/WS1761/0029; LAVENTAIR ELLIPTA (CAP) - EMEA/H/C/003754/WS1761/0032

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of the final report from study WWE117397 (listed as a category 3 study in the RMP): a retrospective longitudinal non-interventional observational study of new users of inhaled umeclidinium/vilanterol (UMEC/VI) or new users of inhaled umeclidinium (UMEC) or new users of long-acting bronchodilators (LABD) in the primary care setting

Action: For adoption of PRAC Assessment Report

7.4.13. Zoledronic acid - ACLASTA (CAP) - EMEA/H/C/000595/II/0074/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 4.8 of the SmPC in order to update the safety information regarding acute phase reactions as requested in the conclusions of post-authorisation measure LEG 0037 on 'rheumatological/immune-mediated syndrome (RIMS)' finalised in September 2019; 2) update of section 5.1 of the SmPC in following the assessment of 24 month data from paediatric extension study 2337E1: a one year, multicentre, open-label extension to study CZOL446H2337 to evaluate safety and efficacy of zoledronic acid twice yearly in osteoporotic children treated with glucocorticoids submitted in accordance with Article 46. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

Action: For adoption of PRAC Assessment Report

[28] Anti-Rheumatic Therapy In Sweden (Swedish biologics register)

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

7.5.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 024.12

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Annual report 2019 on adverse events and/or lack of efficacy, immunological data, follow-up growth disturbances in children and data on urinary hexose tetrasaccharide (Hex4) from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status. The registry aims at detecting adverse events and/or lack of efficacy in patients, and at collecting immunological data, and follow-up growth disturbances in children

Action: For adoption of advice to CHMP

7.5.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 025.12

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Annual report 2019 on data on patients with renal or hepatic insufficiency from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status. The registry aims at detecting adverse events and/or lack of efficacy in patients, and at collecting immunological data, and follow-up growth disturbances in children

Action: For adoption of advice to CHMP

7.5.3. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 017.5

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Third interim report for study ALIROC07997: a PASS using healthcare databases to monitor the safety of Praluent (alirocumab) in patients affected with the human immunodeficiency virus (HIV) (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.5.4. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/ANX 006.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Interim results of DAA-PASS study: a non-interventional imposed study on recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients

after direct-acting antiviral (DAA) therapy in order to estimate the risk of early HCC recurrence associated with DAA therapy exposure compared to no DAA therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438) [final study report expected in Q2 2021]

Action: For adoption of advice to CHMP

7.5.5. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/ANX 038.11

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Sixth annual interim report for study CICL670E2422: an observational, multicentre cohort study to evaluate the long-term exposure and safety of deferasirox in the treatment of paediatric non-transfusion dependent thalassaemia patients over 10 years old for whom deferoxamine is contraindicated or inadequate

Action: For adoption of advice to CHMP

7.5.6. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/MEA 062

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Biennal interim report for study M11-001(aHUS registry): an observational, non-interventional multicentre, multinational study to retrospectively and prospectively collect information on the long-term safety and effectiveness of eculizumab in patients with atypical hemolytic-uremic syndrome (aHUS) who have received or continue to receive eculizumab

Action: For adoption of advice to CHMP

7.5.7. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/ANX 005.1

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Interim results of DAA-PASS study: a non-interventional imposed study on recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAA) therapy in order to estimate the risk of early HCC recurrence associated with DAA therapy exposure compared to no DAA therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438) [final study report expected in Q2 2021]

Action: For adoption of advice to CHMP

7.5.8. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 005.2

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

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

Action: For adoption of advice to CHMP

7.5.9. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/MEA 005.2

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

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

Action: For adoption of advice to CHMP

7.5.10. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 002.2

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

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

Action: For adoption of advice to CHMP

7.5.11. Eribulin - HALAVEN (CAP) - EMEA/H/C/002084/MEA 024

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: Interim results for study E7389-M044-504 (IRENE): an observational, post-authorisation, single-arm, prospective, multicentre cohort study to characterise and determine the incidence of eribulin-induced peripheral neuropathy (PN), and the frequency and time to resolution of eribulin-induced PN in adult patients treated with eribulin in a real-

life setting with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease

Action: For adoption of advice to CHMP

7.5.12. Florbetaben (^{18}F) - NEURACEQ (CAP) - EMEA/H/C/002553/MEA 001.9

Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Martin Huber

Scope: Second interim report for study FBB-01_03_13 (PASS 2): a non-interventional/observational, cross-sectional, retrospective, multicentre, multi-country registry to observe usage pattern, safety and tolerability of the diagnostic agent NeuraCeq (florbetaben (^{18}F)) in European clinical practice [final clinical study report (CSR) expected in Q2/2020]

Action: For adoption of advice to CHMP

7.5.13. Glecaprevir, pibrentasvir - MAVIRET (CAP) - EMEA/H/C/004430/ANX 001

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Interim results of DAA-PASS study: a non-interventional imposed study on recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAA) therapy in order to estimate the risk of early HCC recurrence associated with DAA therapy exposure compared to no DAA therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438) [final study report expected in Q2 2021]

Action: For adoption of advice to CHMP

7.5.14. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/LEG 188.6

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Annual reports for 2018 and 2019 on a review of second primary malignancies (SPM), including a data analysis plan, in order to compare incidence rates of SPM among patients treated with Glivec (imatinib) with expected incidence based on the rates among the general population, including MAH's response to LEG 188.5 on annual report for 2017 as per the request for supplementary information (RSI) adopted in March 2018

Action: For adoption of advice to CHMP

7.5.15. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/ANX 191.8

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Sixth progress report for study CSTI571I2201: a European observational registry collecting efficacy and safety data in newly diagnosed paediatric Philadelphia positive (Ph+) acute lymphoblastic leukaemia (ALL) patients treated with chemotherapy + imatinib ± haematopoietic stem cell treatment (±HSCT)

Action: For adoption of advice to CHMP

7.5.16. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/MEA 005.2

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Third annual progress report for a patient registry of lixisenatide use in adult patients with type 2 diabetes mellitus (T2DM) (listed as a category 3 study in the RMP) in order to monitor the occurrence of events of interest including acute pancreatitis, pancreatic cancer and thyroid cancer, especially medullary carcinoma of the thyroid, among adult T2DM patients treated with lixisenatide using data from national registers and databases in Italy and Belgium [final report expected in December 2020] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.5.17. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/ANX 016.1

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Interim results of DAA-PASS study: a non-interventional imposed study on recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAA) therapy in order to estimate the risk of early HCC recurrence associated with DAA therapy exposure compared to no DAA therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438) [final study report expected in Q2 2021]

Action: For adoption of advice to CHMP

7.5.18. Lixisenatide - LYXUMIA (CAP) - EMEA/H/C/002445/MEA 008.4

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Annika Folin

Scope: Third annual progress report for a patient registry of lixisenatide use in adult patients with type 2 diabetes mellitus (T2DM) (listed as a category 3 study in the RMP) in order to monitor the occurrence of events of interest including acute pancreatitis, pancreatic cancer and thyroid cancer, especially medullary carcinoma of the thyroid, among adult T2DM patients treated with lixisenatide using data from national registers and databases in Italy and Belgium [final report expected in December 2020] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.5.19. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.3

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: First progress report for study A-LUT-T-E02-402 (SALUS study) (listed as a category 3 study in the RMP): an international post-authorisation safety registry to assess the long-term safety of Lutathera (lutetium (^{177}Lu)) for unresectable or metastatic, somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs) [final clinical study report (CSR) expected in December 2025]

Action: For adoption of advice to CHMP

7.5.20. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/LEG 006

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Study progress report for PASS NN7999-4031 : a non-interventional study in male haemophilia B patients receiving nonacog beta pegol (N9-GP) prophylaxis treatment to investigate the potential effects of PEG accumulation in the choroid plexus of the brain and other tissues/organs

Action: For adoption of advice to CHMP

7.5.21. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/ANX 006.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Interim results of DAA-PASS study: a non-interventional imposed study on recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAA) therapy in order to estimate the risk of early HCC recurrence associated with DAA therapy exposure compared to no DAA therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438) [final study report expected in Q2 2021]

Action: For adoption of advice to CHMP

7.5.22. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/ANX 001.2

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Second annual interim study report for study P15-11: a multicentre, observational PASS to document the drug utilisation of Wakix (pitolisant) and to collect information on the

safety of Wakix (pitolisant) when used in routine medical practice [final results expected in 2023] (from opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.5.23. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/ANX 023.1

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Interim results of DAA-PASS study: a non-interventional imposed study on recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAA) therapy in order to estimate the risk of early HCC recurrence associated with DAA therapy exposure compared to no DAA therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438) [final study report expected in Q2 2021]

Action: For adoption of advice to CHMP

7.5.24. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/ANX 009.1

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Interim results of DAA-PASS study: a non-interventional imposed study on recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAA) therapy in order to estimate the risk of early HCC recurrence associated with DAA therapy exposure compared to no DAA therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438) [final study report expected in Q2 2021]

Action: For adoption of advice to CHMP

7.5.25. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/ANX 004

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Interim results of DAA-PASS study: a non-interventional imposed study on recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAA) therapy in order to estimate the risk of early HCC recurrence associated with DAA therapy exposure compared to no DAA therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438) [final study report expected in Q2 2021]

Action: For adoption of advice to CHMP

7.5.26. Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/MEA 002.2

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual interim report for study VX17-661-117 (study 117) (listed as a category 3 study in the RMP): an observational cohort study on utilisation patterns and real-world effects of tezacaftor and ivacaftor combination therapy (TEZ/IVA) in patients with cystic fibrosis (CF) [final report expected in December 2023] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.5.27. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/ANX 002.1

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Interim report for study 156-12-299: a non-interventional PASS to investigate the risks of hepatotoxicity, basal cell carcinoma and glaucoma associated with the use of Jinarc (tolvaptan). In addition, the study investigates pregnancy outcomes in patients treated with Jinarc (tolvaptan), patterns of medicinal product utilisation especially with regards to off-label use and use in patients over 50 years old as well as adverse drug reactions (ADRs) associated with long term use of Jinarc (tolvaptan) [final clinical study report (CSR) expected by: Q4/2022]

Action: For adoption of advice to CHMP

7.5.28. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.6

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Annual study progress report and first interim analysis report for study P16-562 (listed as a category 3 study in the RMP): a prospective observational study to assess the long-term safety profile of venetoclax in a Swedish cohort of chronic lymphocytic leukaemia (CLL) patients

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/MEA 062

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Feasibility report for an international, exploratory, retrospective non-interventional

study to collect long-term safety data including malignancies in children with growth failure who have received at least 3 years of Increlex (mecasermin) therapy and followed at least 5 years after the end of Increlex (mecasermin) treatment (from variation II/60 concluded in November 2019)

Action: For adoption of advice to CHMP

7.6.2. Melatonin - SLENYTO (CAP) - EMEA/H/C/004425/REC 002

Applicant: RAD Neurim Pharmaceuticals EEC SARL

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: First annual French 'recommendation temporaire d'utilisation (RTU)' report on special temporary recommendation of use for Circadin (melatonin) 2-6 mg in the autism spectrum disorder (ASD) and neurogenetic 6-18 year old population for the period from October 2015 to July 2019

Action: For adoption of advice to CHMP

7.6.3. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/MEA 060.2

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 060.1 [six-monthly summary report of medication error events reported with the on body injector in the EU market, as requested in the conclusions of variation II/093/G finalised in February 2018] as per the request for supplementary information (RSI) adopted in October 2019

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

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

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

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

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Cholic acid - KOLBAM (CAP) - EMEA/H/C/002081/S/0031 (with RMP)

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Agni Kapou

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Aegerion Pharmaceuticals B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/S/0055 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ghania Chamouni

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/R/0006 (without RMP)

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/R/0055 (without RMP)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Aripiprazole - ARIPIPRAZOLE SANDOZ (CAP) - EMEA/H/C/004008/R/0014 (without RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Zentiva, k.s.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Duloxetine - DULOXETINE ZENTIVA (CAP) - EMEA/H/C/003935/R/0009 (with RMP)

Applicant: Zentiva k.s.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/R/0022 (without RMP)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/R/0020 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Isavuconazole - CRESEMBA (CAP) - EMEA/H/C/002734/R/0027 (without RMP)

Applicant: Basilea Pharmaceutica Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: ANPHARM Przedsiebiorstwo Farmaceutyczne S.A.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Pemetrexed - PEMETREXED LILLY (CAP) - EMEA/H/C/004114/R/0011 (with RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ghania Chamouni

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Pregabalin - PREGABALIN ACCORD (CAP) - EMEA/H/C/004024/R/0015 (with RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Sandoz GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Sandoz GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Zentiva k.s.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: AstraZeneca AB

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Željana Margan Koletić

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.16. Sufentanil - ZALVISO (CAP) - EMEA/H/C/002784/R/0016 (without RMP)

Applicant: Grunenthal GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.17. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/R/0045 (without RMP)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.18. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/R/0037 (without RMP)

Applicant: Correvio

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Olanzapine - OLANZAPINE APOTEX (CAP) - EMEA/H/C/001178/II/0037

Applicant: Apotex Europe BV

PRAC Rapporteur: Kimmo Jaakkola

Scope: PRAC consultation on a type II variation updating sections 4.4 and 4.8 of the SmPC in order to add information regarding the risk of metabolic syndrome (MetS) with the use of olanzapine (and all antipsychotics), based on review of the available data from Apotex global safety database, EudraVigilance and literature, on request of CHMP

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Fentanyl[29] (NAP) - NL/H/3915/II/007/G

Applicant(s): Janssen-Cilag B.V. (Durogesic)

PRAC Lead: Liana Gross-Martirosyan

Scope: PRAC consultation on a variation (part of an ongoing grouped variation procedure) on an update section 4.4 of the SmPC on drug dependence and potential for abuse regarding the increased risk of developing tolerance, physical dependence, or psychological dependence to opioids in individuals with a personal or family history of substance abuse or mental illness, on request of the Netherlands

Action: For adoption of advice to Member States

11.1.2. Paracetamol (NAP) - IE/H/0835/001/II/056/G, PA0678/037/001

Applicant(s): GSK Consumer Healthcare (Paracetamol + Pseudoephedrine 500mg/30 mg, Panadol with Caffeine 500mg/65 mg)

PRAC Lead: Rhea Fitzgerald

Scope: PRAC consultation on national variations on proposed amendments of the product information aimed at strengthening the risk minimisation measures for paracetamol regarding the risk of hepatotoxicity at therapeutic doses, on request of Ireland

Action: For adoption of advice to Member States

[29] Transdermal patch

11.2. Other requests

11.2.1. Bupropion (NAP) - NL/H/PSUFU/00000461/201812

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: PRAC consultation on a PSUR follow-up (PSU FU) procedure on increased sexual function with bupropion use including all available information including cases published in the literature, data from non-clinical studies, clinical and epidemiological studies and post marketing spontaneous, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure (PSUSA/00000461/201812) concluded in September 2019, on request of the Netherlands

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. EudraVigilance data analysis system (EVDAS) - training for National Competent Authorities (NCAs)

Action: For discussion

12.4.2. PRAC strategic review and learning meeting (SRLM) under the Croatian presidency of the European Union (EU) Council - Split, Croatia, 22-24 April 2020 - Agenda

PRAC lead: Nikica Mirošević Skvrce, Željana Margan Koletić

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Additional monitoring

None

12.12.2. Additional monitoring – status of lenalidomide-containing product(s)

Action: For discussion

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

Action: For adoption

12.12.4. Management and reporting of adverse reactions to medicinal products

None

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. EudraVigilance – annual report 2019

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.14.3. Good pharmacovigilance practice (GVP) module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' – request for input on terminology

PRAC lead: Sabine Straus

Action: For discussion

12.15. Post-authorisation safety studies (PASS)

12.15.1. EU post-authorisation safety studies (EU PASS) register - notification of imposed studies registered in the EU PASS Register to Member States

Action: For discussion

12.15.2. Post-authorisation safety studies – non-imposed PASS

None

12.15.3. Post-authorisation safety studies – non-imposed PASS

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Drug-induced hepatotoxicity – draft PRAC guidance

PRAC lead: Menno van der Elst, Martin Huber

Action: For discussion

12.20.2. EMA new organisational structure for human medicines division

Action: For discussion

12.20.3. Medical Dictionary for Regulatory Activities (MedDRA) points to consider group – call for EU expert nomination

Action: For discussion

12.20.4. Serious cutaneous adverse reactions (SCARs) - PRAC guidance update

PRAC lead: Sabine Straus, Zane Neikena

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/