04 April 2022
EMA/PRAC/142420/2022
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 04-07 April 2022

Chair: Sabine Straus – Vice-Chair: Martin Huber

04 April 2022, 10:30 – 19:30, via teleconference

05 April 2022, 08:30 – 19:30, via teleconference

06 April 2022, 08:30 – 19:30, via teleconference

07 April 2022, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

21 April 2022, 09:00 – 12:00, via teleconference

Disclaimers

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

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

Note on access to documents

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

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Table of contents

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 04-07 April 2022. See April 2022 PRAC minutes (to be published post May 2022 PRAC meeting).

1.2. Agenda of the meeting on 04-07 April 2022

Action: For adoption

1.3. Minutes of the previous meeting on 07-10 March 2022

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. Terlipressin (NAP) - EMEA/H/A-31/1514

Applicant(s): various

PRAC Rapporteur: Krõõt Aab; PRAC Co-rapporteur: Anette Kirstine Stark

Scope: Review of the benefit-risk balance following notification by Denmark 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

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of corneal graft rejection

Action: For adoption of PRAC recommendation

EPITT 19791 – New signal

Lead Member State(s): BE

4.1.2. Elasomeran - SPIKEVAX (CAP)

Applicant: Moderna Biotech Spain, S.L.

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

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of corneal graft rejection

Action: For adoption of PRAC recommendation

EPITT 19792 – New signal

Lead Member State(s): DK

4.1.3. Rivaroxaban - RIVAROXABAN ACCORD (CAP), RIVAROXABAN MYLAN (CAP), XARELTO (CAP); NAP

Applicant(s): Accord Healthcare S.L.U. (Rivaroxaban Accord), Bayer AG (Xarelto), Mylan Ireland Limited (Rivaroxaban Mylan)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of pemphigoid

Action: For adoption of PRAC recommendation

EPITT 19785 – New signal

Lead Member State(s): SE

4.1.4. Tozinameran - COMIRNATY (CAP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of corneal graft rejection

Action: For adoption of PRAC recommendation

EPITT 19789 – New signal

Lead Member State(s): NL

4.2. New signals detected from other sources

4.2.1. Gemtuzumab ozogamicin – MYLOTARG (CAP)

Applicant(s): Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of atypical haemolytic reactions

Action: For adoption of PRAC recommendation

EPITT 19788 – New signal

Lead Member State(s): PT

4.3. Signals follow-up and prioritisation

4.3.1. Abatacept – ORENCIA (CAP) - EMEA/H/C/000701/SDA/068

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of acute respiratory distress syndrome (ARDS)

Action: For adoption of PRAC recommendation

EPITT 19751 - Follow-up to December 2021[3]

4.3.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/022

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of optic neuritis

Action: For adoption of PRAC recommendation

EPITT 19747 – Follow-up to December 2021[4]

4.3.3. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/054

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of autoimmune hepatitis

Action: For adoption of PRAC recommendation

EPITT 19750 – Follow-up to December 2021[5]

4.3.4. Tocilizumab – ROACTEMRA (CAP) - EMEA/H/C/000955/SDA/060

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of encephalopathy including posterior reversible encephalopathy syndrome (PRES)

Action: For adoption of PRAC recommendation

EPITT 19731 – Follow-up to November 2021[6]

[3] Held 29 November–02 December 2021
[4] Held 29 November–02 December 2021
[5] Held 29 November–02 December 2021
[6] Held 25-28 October 2021

4.3.5. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/SDA/042

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of autoimmune hepatitis

Action: For adoption of PRAC recommendation

EPITT 19749 – Follow-up to December 2021[7]

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/WS2235/0050; LENVIMA (CAP) - EMEA/H/C/003727/WS2235/0046

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: Update of section 4.8 of the SmPC in order to add colitis as an adverse drug reaction with a frequency 'uncommon' following the outcome of the signal procedure (EPITT 19691) adopted in November 2021. The package leaflets are updated accordingly

Action: For adoption of PRAC Assessment Report

4.4.2. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0044

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.4, 4.8 and 5.1 to add warnings and safety data on serious infections, viral reactivation, non-melanoma skin cancer and fractures. This is based on the final results from study A3921133 (listed as a category 3 study in the RMP): a PASS conducted to evaluate the safety of tofacitinib 5 mg and 10 mg compared to tumour necrosis factor inhibitor (TNFi) in adult subjects aged ≥50 years with moderately or severely active rheumatoid arthritis (RA) and with at least 1 additional cardiovascular (CV) risk factor, as requested in the outcome of the signal procedure (EPITT 19382) adopted in June 2021 (SDA 016). The package leaflet is updated accordingly. The RMP (version 21.1) is also updated in accordance. In addition, the MAH took the opportunity to update the outer carton (section 4 for oral solution) to include a total volume of 240 mL as requested in the conclusions of procedure X/0024/G adopted in June 2021

Action: For adoption of PRAC Assessment Report

[7] Held 29 November–02 December 2021

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Asciminib - EMEA/H/C/005605, Orphan

Applicant: Novartis Europharm Limited

Scope: Treatment of Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP)

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

5.1.2. Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - EMEA/H/C/006019

Scope: Active immunisation for prevention of coronavirus disease-2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older

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

5.1.3. Dimethyl fumarate - EMEA/H/C/005963

Generic

Scope: Treatment of multiple sclerosis

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

5.1.4. Efgartigimod alfa - EMEA/H/C/005849, Orphan

Applicant: Argenx

Scope: Treatment of generalised myasthenia gravis (gMG)

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

5.1.5. Lenacapavir - EMEA/H/C/005638

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

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

5.1.6. Maribavir - EMEA/H/C/005787, Orphan

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

Scope: Treatment of cytomegalovirus (CMV) infection

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

5.1.7. Molnupiravir - EMEA/H/C/005789

Scope: Treatment of coronavirus disease 2019 (COVID-19)

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

5.1.8. Ranibizumab - EMEA/H/C/005019

Scope: Treatment of neovascular (wet) age-related macular degeneration (AMD), visual impairment due to diabetic macular oedema (DME), proliferative diabetic retinopathy (PDR), visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO) and visual impairment due to choroidal neovascularisation (CNV)

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

5.1.9. Sorafenib - EMEA/H/C/005921

Scope: Treatment of hepatocellular carcinoma and renal cell carcinoma

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

5.1.10. Surufatinib - EMEA/H/C/005728

Scope: Treatment of progressive neuroendocrine tumours

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. Bulevirtide - HEPCLUDEX (CAP) - EMEA/H/C/004854/II/0012, Orphan

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of an updated RMP (version 1.2) in order to replace non-interventional study MYR-HDV (listed as a category 3 study in the RMP): a long-term safety and efficacy registry, with interventional registry study GS-US-589-6206: a registry study of treatment with bulevirtide in participants with chronic hepatitis D infection. In addition, the MAH took the opportunity to update the information in the RMP on epidemiology, clinical trial exposure and post-authorisation experience

Action: For adoption of PRAC Assessment Report

5.2.2. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/II/0029

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of an updated RMP (version 3.0) in line with the product information changes implemented following the assessment of PSUR single assessment (PSUSA) procedure (PSUSA/00010758/202103) adopted in October 2021 with regards to severe

hypersensitivity reactions. The MAH took the opportunity to update PASS details according to the latest approved PASS protocols, namely the study on the 'assessment of pregnancy outcomes in patients treated with Ajovy (fremanezumab): pregnancy registry' and the study on the 'assessment of pregnancy outcomes in patients treated with Ajovy (fremanezumab): pregnancy database study'

Action: For adoption of PRAC Assessment Report

5.2.3. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/II/0048

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 9) to reflect the proposal to stop the enrolment and to close the pregnancy registry known as mepolizumab pregnancy exposure study 200870 (listed as category 3 study in the RMP): a phase 4, prospective, observational, exposure cohort study of pregnancy outcomes in women. The application also includes details of the proposed enhanced data collection for all pregnancies reported as an alternative

Action: For adoption of PRAC Assessment Report

5.2.4. Mercaptamine - CYSTADROPS (CAP) - EMEA/H/C/003769/II/0023, Orphan

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: Submission of an updated RMP (version 1.4) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and to remove 'patients with other ocular co-morbidities' and 'patients receiving concomitant treatment with ophthalmic products containing benzalkonium chloride' as missing information from the list of safety concerns

Action: For adoption of PRAC Assessment Report

5.2.5. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/II/0046

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Submission of an updated RMP (version 11.0) in line with the outcome of the renewal procedure R/0025 finalised in May 2019 to remove the following safety concerns: 1) important identified risks: diarrhoea, liver enzyme and bilirubin elevations including drug-induced liver injury (DILI), bleeding, myocardial infarction; 2) important potential risks: venous thromboembolism, arterial thromboembolism excluding myocardial infarction, perforation, hepatic failure, treatment of pregnant women and teratogenicity, cardiac failure; 3) missing information: treatment of patients with moderate or severe hepatic impairment (Child Pugh B/C), treatment of black patients, treatment of patients with healing wounds, treatment of patients with severe renal impairment or end-stage renal disease, treatment of patients receiving full-dose therapeutic anticoagulation and treatment of breastfeeding women. In addition, the anatomical therapeutic chemical (ATC) code and post-marketing exposure are updated

Action: For adoption of PRAC Assessment Report

5.2.6. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/II/0010

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of an updated RMP (version 2.0) in order to remove 'immunogenicity' as an important identified risk revision 2 of GVP module V on 'Risk management systems', EMA guidance on immunogenicity assessment, and the available non-clinical, clinical and post-marketing data. In addition, the MAH took the opportunity to add 'cardiac arrythmia' as an important potential risk to the RMP and to update the protocol for the ongoing study OP0004: a European non-interventional PASS related to serious cardiovascular events of myocardial infarction and stroke, and all-cause mortality for romosozumab by the EU-ADR Alliance to include cardiac arrhythmias as specific events to monitor, and include a targeted follow-up questionnaire (FUQ) related to cardiac arrhythmias, in line with the outcome of the signal procedure on cardiac arrhythmia (EPITT 19629) adopted in May 2021. The MAH took also the opportunity to introduce minor changes in the PASS protocols of studies OP0004, OP0005: a European non-interventional PASS related to adherence to the risk minimisation measures for romosozumab by the EU-ADR Alliance, and OP0006: European non-interventional PASS related to serious infections for romosozumab by the EU-ADR Alliance

Action: For adoption of PRAC Assessment Report

5.2.7. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS2185/0041; NEPARVIS (CAP) - EMEA/H/C/004343/WS2185/0039

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 3.0) as requested in the outcome of variation WS1830 completed in November 2020. In addition, the following changes have been introduced: 1) change to the agreed milestone for study CLCZ696B2320 (listed as a category 3 study in the RMP): a multicentre, randomized, double-blind, active-controlled study to evaluate the effects of sacubitril/valsartan (LCZ696) compared to valsartan on cognitive function as assessed by comprehensive neurocognitive battery and brain amyloid plaque deposition as assessed by positron emission tomography (PET) imaging in patients with chronic heart failure with preserved ejection fraction; 2) update to the date for the submission of the final report for study CLCZ696B2320 from 'Q1 2022' to 'Q1 2023', 3) update of the presentation of important identified risks and important potential risks; 4) update to exposure and post-marketing data provided for the data lock point (DLP) of PSUR#9 (31 July 2021)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/II/0001

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.4 and 4.8 of the SmPC based on updated safety data from the full cumulative pool from ongoing long-term extension study B7451015: a phase 3 multicentre, long-term extension study investigating the efficacy and safety of abrocitinib, with or without topical medications, administered to subjects aged 12 years and older with moderate to severe atopic dermatitis. The RMP (version 1.0) is updated accordingly. In addition, MAH took the opportunity to implement editorial changes in the SmPC and to update the contact details of the local representatives in the package leaflet

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

5.3.2. Adalimumab - IMRALDI (CAP) - EMEA/H/C/004279/II/0048/G

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) introduction of an additional concentration of 40 mg/0.4 mL for the solution for subcutaneous injection in pre-filled syringe (PFS) and pre-filled pen (PFP); 2) Change in the composition of excipients for the proposed 40 mg/0.4 mL solution for injection in PFS and PFP; 3) variations to introduce a change in the number of units in a pack within the range of the currently approved pack sizes. The RMP (version 7.1) is updated accordingly. The applicant took the opportunity to change the registration mark '®', which is adjacent to the brand name Imraldi, to the trademark '™'

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

5.3.3. Baloxavir marboxil - XOFLUZA (CAP) - EMEA/H/C/004974/X/0008/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Grouped variations consisting of: 1) extension application to introduce a new pharmaceutical form associated with new strength (2 mg/mL granules for oral suspension); 2) extension of indication to add a paediatric indication applicable to the new presentation, as well as to all approved presentations (EU/1/20/1500/001 and 002). The RMP (version 2.0) is updated in accordance

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

5.3.4. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0029/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of: 1) extension of indication to include treatment of severe alopecia areata in adult patients. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 12.1) are updated in accordance; 2) update of the RMP (version 12.1) regarding study I4V-MC-B011 (listed as a category 3 study in the RMP): a retrospective cohort study to assess the safety of baricitinib compared with other therapies used in the treatment of rheumatoid arthritis in Nordic countries to change the end of data collection for the atopic dermatitis cohort from 'December 2026' to 'December 2027' and the subsequent final study report milestone from 'December 2027' to 'December 2028'

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

5.3.5. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0079/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) changes to the manufacturing process of the biological active substance belatacept 2) change to in-process tests or limits applied during the manufacture of the active substance; 3) update of the RMP (version 20.0) to include the new maintenance dose, the new potential risk of medication errors and a Direct healthcare professional communication (DHPC) listed as an additional risk minimisation measure (in line with the outcome of CHMP procedure II/0065/G dated November 2021)

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

5.3.6. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/II/0028, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of adverse drug reactions, to split immunogenicity data into paediatric and adult populations and to update clinical efficacy in paediatric patients upon request by the CHMP, following procedures P46/006, P46/007 and variations II/04 and II/10/G finalised in October 2019 and July 2020 respectively, based on the final results from: 1) study UX023-CL201: a randomised, open-label, dose finding, phase 2 study to assess the pharmacodynamics and safety of KRN23 (burosumab) in paediatric patients with X-linked hypophosphatemia (XLH); 2) study UX023-CL205: an open-label, phase 2 study to assess the safety, pharmacodynamics, and efficacy of KRN23 in children from 1 to 4 years old with XLH; 3) study UX023-CL301: randomized, open-label, phase 3 study to assess the efficacy and safety of krn23 versus oral phosphate and active vitamin D treatment in paediatric patients with XLH. In addition, the MAH proposed to delete the remaining specific obligation (SO) for study UX023-CL205 from Annex II, and to request a switch from a conditional marketing authorisation (MA) to standard MA. 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

5.3.7. Caplacizumab - CABLIVI (CAP) - EMEA/H/C/004426/II/0035, Orphan

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on increased risk of bleeding and to add blood and lymphatic system disorders to the list of adverse drug reactions (ADRs) with a frequency not known based on a safety evaluation report. The package leaflet and the RMP (version 2.0) are updated accordingly

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

5.3.8. Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/II/0028

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include cemiplimab in combination with platinum-based chemotherapy for the first-line treatment of adult patients with locally advanced non-small-cell lung carcinoma (NSCLC) who are not candidates for definitive chemoradiation or metastatic NSCLC with no epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK) or c-Ros oncogene 1 receptor tyrosine kinase (ROS1) aberrations. As a consequence, sections 4.1, 4.4, 4.8, and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.9. Corifollitropin alfa - ELONVA (CAP) - EMEA/H/C/001106/II/0061

Applicant: Organon N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of adolescent males (14 to less than 18 years) with hypogonadotropic hypogonadism in combination with human chorionic gonadotropin (hCG) based on final results of paediatric study P043: an open-label, non-comparative, multicentre safety and efficacy study of corifollitropin in association with hCG in male adolescents with hypogonadotropic hypogonadism, part of the paediatric investigation plan (PIP). As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 9.2) are updated in accordance. In addition, the MAH took the opportunity to implement some minor editorial and formatting changes throughout the product information

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

5.3.10. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[8]) - EMEA/H/W/002168/II/0015/G

Applicant: International Partnership for Microbicides Belgium AISBL

[8] 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: Jan Neuhauser

Scope: Grouped variations consisting of submission of four addenda from studies (listed as category 3 studies in the RMP): 1) IPM 007 (RING study): a phase 3, randomised study exploring dapivirine ring long-term safety and efficacy; 2) study MTN-015: a multisite, prospective, observational cohort study of women following human immunodeficiency virus type 1 (HIV-1) seroconversion in microbicide trials of antiretroviral (ARV)-based microbicides or oral pre-exposure prophylaxis (PrEP); 3) studies IPM 032 and MTN-025: phase 3b open-label extension (OLE) dapivirine ring trials. The data presented in the addenda are the results of retrospective next generation sequencing (NGS) and phenotype susceptibility testing on blood samples to further assess the potential development of non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance in women with unrecognized or acute HIV-1 infection. The RMP (version 0.9) is updated accordingly. Additionally, the MAH took the opportunity to update the EMA on other commitments outlined in the RMP as additional risk minimisation measures. These include the development of a healthcare professional guide (HCP guide) and a user guide with agreed objectives and key messages

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

5.3.11. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[9]) - EMEA/H/W/002168/II/0016

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser

Scope: Update of Annex II in order to replace the current post-authorisation efficacy study (PAES) IPM 055 (listed as a category 1 study in the RMP): a phase 4, open label, multicentre efficacy trial in healthy human immunodeficiency virus (HIV)-negative young women aged 18-25 years, with the implementation study: 'dapivirine vaginal ring implementation in a real-world setting in young women. The RMP (version 0.9) is updated accordingly

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

5.3.12. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0082/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped variations consisting of: 1) submission of the final report from study CICL670F2202 (Calypso study) (listed as a category 3 study in the RMP): a randomized, open-label, multicentre, two arm, phase 2 study to evaluate treatment compliance, efficacy and safety of deferasirox (granules) in paediatric patients with iron overload; 2) removal of the risk of 'medication error' from the RMP and of the information related to the discontinuation of the dispersible tablets in the EU. The RMP (version 20.0) is updated accordingly

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

[9] 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)

5.3.13. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0041

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include first-line treatment, with durvalumab in combination with tremelimumab and platinum-based chemotherapy, of adults with metastatic non-small-cell lung carcinoma (NSCLC) with no sensitizing epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumour aberrations, based on final results from study D419MC00004 (POSEIDON): a phase 3, randomised, multicentre, open-label, comparative global study to determine the efficacy and safety of tremelimumab and durvalumab or durvalumab in combination with platinum based chemotherapy for first-line treatment in patients with metastatic NSCLC. 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 is updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2). The RMP (version 5.1) is updated accordingly

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

5.3.14. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/II/0034

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study MK-5172-017 (listed as a category 3 study in the RMP): a long-term follow-up study to evaluate the durability of virologic response and/or viral resistance patterns of subjects with chronic hepatitis C who have been previously treated with Zepatier (elbasvir/grazoprevir) in a prior clinical trial (in fulfilment of MEA 002.1). The RMP (version 5.1) is updated accordingly

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

5.3.15. Eltrombopag - REVOLADE (CAP) - EMEA/H/C/001110/II/0068

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of adult patients with primary immune thrombocytopenia (ITP) who are refractory to other treatments (e.g. corticosteroids, immunoglobulins) irrespective of time since initial diagnosis, based on an ad-hoc analysis of study TAPER (CETB115J2411): an ongoing phase 2, open-label, prospective, single-arm study in adult ITP patients who are refractory or relapsed after first-line steroids. As a consequence, sections 4.1 and 5.1 of the SmPC have been updated. In addition, the MAH took the opportunity to make some minor amendments in section 4.8 of the SmPC for increased consistency. The RMP (version 54.0) is updated accordingly

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

5.3.16. Emtricitabine, tenofovir alafenamide - DESCOVY (CAP) - EMEA/H/C/004094/II/0057

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the clinical study report and supporting modular summaries for study GS-US-311-1269: a phase 2/3, open label, multi-cohort switch study to evaluate emtricitabine/tenofovir alafenamide (F/TAF) in human immunodeficiency virus type 1 (HIV-1) infected children and adolescents virologically suppressed on a two nucleoside reverse transcriptase inhibitors (NRTI) containing regimen in fulfilment of the milestone for the category 3 additional pharmacovigilance activity to address long-term safety information in adolescents as missing information. The RMP (version 6.1) is updated accordingly

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

5.3.17. Eptacog alfa (activated) - NOVOSEVEN (CAP) - EMEA/H/C/000074/II/0116

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of severe postpartum haemorrhage for NovoSeven (eptacog alfa). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 8.0) are updated accordingly

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

5.3.18. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0073

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include the treatment of adolescents and children aged 10 years and above based on the results from study BCB114 (D5551C00002): a phase 3, double-blind, placebo-controlled, randomised, multicentre study to assess the safety and efficacy of exenatide once weekly in adolescents with type 2 diabetes (T2DM), which was initially submitted and assessed by the CHMP as part of post-authorisation measure (PAM) P46 028. 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 35s1) are updated in accordance

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

5.3.19. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0012, Orphan

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of seizures associated with Lennox-Gastaut syndrome as an add on therapy to other anti-epileptic medicines for patients 2 years of age and older. As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 2.3) are updated accordingly

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

5.3.20. Insulin lispro - LYUMJEV (CAP) - EMEA/H/C/005037/II/0014

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include the treatment of diabetes mellitus in adolescents and children aged 1 year and above, based on the final results from study I8B-MC-ITSB: a pivotal phase 3 study designed to evaluate the safety and efficacy of Lyumjev (insulin lispro) compared to Humalog (insulin lispro) in combination with basal insulin in children and adolescent patients with type 1 diabetes mellitus (T1DM). 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 12.1) are updated in accordance. In addition, the MAH took the opportunity to implement minor editorial and linguistic changes in the product information. As part of the application, the MAH is also requesting one additional year of market protection

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

5.3.21. Mercaptamine - PROCYSBI (CAP) - EMEA/H/C/002465/X/0035, Orphan

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to introduce a new pharmaceutical form associated with two new strengths (75 and 300 mg gastro-resistant granules). The RMP (version 7.2) is updated in accordance

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

5.3.22. Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/X/0039/G

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped variations consisting of: 1) extension application to introduce a new pharmaceutical form associated with new strength (8 mg/mL prolonged-release granules for oral suspension); 2) extension of indication to include treatment of neurogenic detrusor overactivity (NDO) in paediatric patients aged 3 to less than 18 years. The RMP (version 9.0) is updated in accordance

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

5.3.23. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/II/0038

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC to include data from LEOPOLD kids part B: a long-term efficacy open-label programme in severe haemophilia A disease (previously submitted as an Art 46; an addendum on biomarker data is included in this submission) and extension study results. In addition, an editorial revision in section 4.2 and a clarification in section 6.5 of the SmPC are proposed. The package leaflet is updated accordingly. The MAH

took the opportunity to correct a typo in the Greek product information. The RMP (version 4.1) is updated and brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

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

5.3.24. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0051/G

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include adjuvant treatment of breast cancer for Lynparza (olaparib) tablets. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. In addition, section 4.8 of the SmPC for Lynparza (olaparib) hard capsules is revised based on the updated safety data analysis. The package leaflet and the RMP (version 23) are updated accordingly

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

5.3.25. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0053

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of adults with metastatic castration resistant prostate cancer (mCRPC) with olaparib in combination with abiraterone and prednisone or prednisolone, based on the results of the pivotal study D081SC00001 (PROpel study): a phase 3, randomised, double-blind, placebo-controlled, multicentre study evaluating olaparib vs placebo in combination with abiraterone as first line treatment for men with mCRPC, and supportive evidence from study D081DC00008 (study 8): a randomised, double-blind, placebo-controlled, multicentre phase 2 study to compare the efficacy, safety and tolerability of olaparib versus placebo when given in addition to abiraterone treatment in patients with mCRPC who have received prior chemotherapy containing docetaxel. Consequently, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC for Lynparza (olaparib) tablets are updated. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza (olaparib) hard capsules are revised based on the updated safety data analysis. The package leaflet and the RMP (version 24) are updated accordingly

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

5.3.26. Palbociclib - IBRANCE (CAP) - EMEA/H/C/003853/II/0037

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of the final report from study A5481027 (listed as a category 3 study in the RMP): a multicentre, randomized, double-blind, phase 3 study of palbociclib plus letrozole versus placebo plus letrozole for the treatment of previously untreated Asian postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor-2 (HER2)-negative advanced breast cancer to evaluate the effect of palbociclib on hyperglycaemia (in fulfilment of MEA 001). The RMP (version 1.8) is updated

accordingly

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

5.3.27. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP) - EMEA/H/C/001206/II/0074

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include use in children from 6 months to <18 years for Adjupanrix (pandemic influenza vaccine (H5N1)) based on the results of the following studies: 1) study H5N1-013: a phase 2, non-randomised, open-label study to evaluate the safety and immunogenicity in children aged 6 to 35 months; 2) study H5N1-032: a phase 3, randomised, open, active-controlled study to evaluate the safety and immunogenicity in children aged 3 to 17 years. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 13) are updated in accordance. Further, the MAH proposed to update section 4.4 with information on sodium and potassium content in line with the excipient guideline, as well as to add some wording on traceability. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2). Finally, the MAH introduced minor editorial changes throughout the product information

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

5.3.28. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - VAXNEUVANCE (CAP) - EMEA/H/C/005477/II/0001

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of infants, children and adolescents from 6 weeks to less than 18 years of age for active immunisation for the prevention of invasive disease, pneumonia and acute otitis media for Vaxneuvance, based on final results from: 1) study V114-008: a phase 2, double-blind, randomized, multicentre trial to evaluate the safety, tolerability, and immunogenicity of V114 (pneumococcal polysaccharide conjugate vaccine (adsorbed)) compared to Prevenar 13 (pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) in healthy infants; 2) seven phase 3 studies (V114-023, V114-024, V114-025, V114-027, V114-029, V114-030, V114-031): interventional studies to evaluate the safety, tolerability and immunogenicity of V114 (pneumococcal polysaccharide conjugate vaccine (adsorbed)) in healthy and immunocompromised infants, children and adolescents. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to include editorial changes in the product information. The RMP (version 1.1) is updated accordingly

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

5.3.29. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0034/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Grouped variations consisting of: 1) update sections 5.1 and 5.2 of the SmPC as a consequence of the submission of the final component of specific obligation (SO) 012 agreed in the renewal procedure of the conditional marketing authorisation (CMA) (R/0015) finalised in April 2021 and listed in Annex II of the product information. This submission includes the adaptive COVID-19 treatment trial (ACTT-1) final sequencing and phenotyping analysis and the full virology report including activity against variants. The package leaflet and the RMP (version 3.1) are updated accordingly

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

5.3.30. Ribociclib - KISQALI (CAP) - EMEA/H/C/004213/II/0035

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final overall survival (OS) analysis from study A2301 (MONALEESA-2) (listed as a category 3 study in the RMP): a phase 3, randomized, double-blind, placebo-controlled, multicentre study of ribociclib in combination with letrozole in postmenopausal women with hormonal receptor + (HR+), human epidermal growth factor receptor-2 negative (HER2-) , locoregionally recurrent or metastatic breast cancer who had not received previous systemic therapy for advanced disease, and based on an updated pooled safety dataset including 1) study MONALEESA-2; 2) study MONALEESA-3: a randomized double-blind, placebo-controlled study of ribociclib in combination with fulvestrant for the treatment of men and postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer who have received no or only one line of prior endocrine treatment; 3) study MONALEESA-7: a phase 3 randomized, double-blind, placebo-controlled study of LEE011 or placebo in combination with tamoxifen and goserelin or a non-steroidal aromatase inhibitor (NSAI) and goserelin for the treatment of premenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer (in fulfilment of MEA 004). The package leaflet and the RMP (version 6.0) is updated accordingly

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

5.3.31. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/X/0020/G

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped variations consisting of: 1) extension application to introduce a new pharmaceutical form (concentrate for solution for infusion), a new strength (600 mg) and a new route of administration (intravenous use); 2) extension of application to add a new strength of 360 mg (150 mg/mL) for risankizumab solution for injection (in cartridge) for subcutaneous use. The new presentations are indicated for the treatment of patients 16 years and older with moderately to severely active Crohn’s disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a

biologic therapy, or if such therapies are not advisable. The RMP (version 4.0) is updated in accordance

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

5.3.32. Risdiplam - EVRYSDI (CAP) - EMEA/H/C/005145/II/0005/G, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Grouped variations consisting of: 1) extension of indication to include treatment of patients below 2 months of age based on interim results from pivotal study BN40703 (RAINBOWFISH): an ongoing phase 2 multicentre, open-label, and single-arm study designed to evaluate the efficacy, safety, tolerability, and pharmacokinetic/pharmacodynamic (PK/PD) of risdiplam in pre-symptomatic infants below 2 months of age who were genetically diagnosed with spinal muscular atrophy (SMA). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, the MAH took the opportunity to make some editorial improvements in the product information; 2) update of Evrysdi (risdiplam) pack configuration. As a consequence, section 6.5 of the SmPC and the labelling are updated; 3) removal of a device. As a consequence, section 6.5 of the SmPC and the labelling are updated. The package leaflet and the RMP (version 1.1) are updated in accordance

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

5.3.33. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/II/0011

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include first-line treatment of rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) based on results from study LIBRETTO-001: an open-label, multicentre, global phase 1/2 study of selpercatinib in patients with RET-altered advanced solid tumours. As a consequence, sections 4.1, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated in accordance

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

5.3.34. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/WS2141/0024; RYBELSUS (CAP) - EMEA/H/C/004953/WS2141/0018

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report from study NN9535-4386 (SUSTAIN-11) (listed as a category 3 study in the RMP): a 52-week, multicentre, multinational, open-label, active controlled, two armed, parallel, randomised trial undertaken to investigate the effect on glycaemic control, body weight, safety and health-related quality of life of once-weekly semaglutide subcutaneous (sc) vs insulin aspart three times daily, both as add-on to metformin and optimised insulin glargine U100 treatment in subjects with inadequately

controlled type 2 diabetes mellitus (T2DM). The RMP (version 7.0) is updated accordingly

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

5.3.35. Setmelanotide - IMCIVREE (CAP) - EMEA/H/C/005089/II/0002/G, Orphan

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Marek Juracka

Scope: Grouped variations consisting of: 1) addition of a new therapeutic indication for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 1.0) are updated accordingly; 2) addition of a new therapeutic indication for the treatment of obesity and the control of hunger associated with genetically confirmed Alström syndrome (AS). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated accordingly. The package leaflet and the RMP (version 1.0) are updated in accordance

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

5.3.36. Tagraxofusp - ELZONRIS (CAP) - EMEA/H/C/005031/II/0009, Orphan

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study 20255431 (CRL-263114) (listed as a category 3 study in the RMP): a non-interventional, post-authorisation study on blood brain barrier (BBB) models in order to determine a potential toxicity biomarker to further investigate the risk of choroid plexus lesions - a characterisation of fixed choroid plexus samples from primate study MPI-2231-007 by immunohistochemistry with diphtheria toxin (DT), interleukin-3 receptor (CD123), interleukin-3 (IL-3) and immunoglobulin G (IgG) (in fulfilment of MEA 002). The RMP (version 2.0) is updated accordingly

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

5.3.37. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/II/0054/G, Orphan

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Grouped variations consisting of: 1) extension of indication to include patients from 4 months corrected gestational aged 1 year and above. Consequently, sections 4.1, 4.2, 4.8, 5.1 and 5.2 are updated. The package leaflet and the RMP (version 9.1) are updated accordingly; 2) update of Annex II-D on 'Conditions or restrictions with regards to the safe and effective use of the medicinal product' to amend the date of completion of the imposed post authorisation study: an international short bowel syndrome registry, from Q3 2031 to Q2 2032. In addition, the MAH took the opportunity to amend the list of local representatives

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

5.3.38. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0046

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of section 5.3 of the SmPC in order to update safety information on reproductive and developmental toxicity based on final study results from study 00655256 (20GR261) (listed as a category 3 study in the RMP): an oral (gavage) juvenile toxicity study of CP-690550 (tofacitinib) in Sprague Dawley rats (in fulfilment of MEA 022). In addition, the MAH took the opportunity to update the contact details of the local representatives in the package leaflet. The RMP (version 23.1) is updated accordingly

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

5.3.39. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/II/0016

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include the treatment of active non-radiographic axial spondyloarthritis (nr-axSpA) in adult patients with objective signs of inflammation who have responded inadequately to non-steroidal anti-inflammatory drugs (NSAIDs) or other conventional therapy based on the final clinical study report from pivotal study M19-944 study 2 (nr-axSpA): a randomized, double-blind, phase 3 study evaluating the long-term safety, tolerability, and efficacy of upadacitinib 15 mg every day (QD) in subjects with nr-axSpA who completed the double-blind period on study drug. 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 8.0) are updated accordingly

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

5.3.40. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/X/0012/G

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Grouped applications consisting of: 1) extension application to add a new strength (45 mg) of the prolonged-release tablets; 2) extension of indication for treatment of adults with moderately to severely active ulcerative colitis who had an inadequate response, lost response or were intolerant to either conventional therapy or a biologic agent. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet, labelling and the RMP (version 6.0) are updated in accordance

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

5.3.41. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/II/0002

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of adult patients with marginal zone

lymphoma (MZL) who have received at least one-prior anti-cluster of differentiation (CD20)-based therapy based on data from 88 patients with relapsed or refractory (R/R) MZL from two ongoing pivotal studies namely: 1) study BGB-3111-214 (MAGNOLIA): a phase 2, open-label, single-arm study designed to evaluate the safety and efficacy of zanubrutinib in patients with R/R MZL; 2) study BGB-3111-AU-003: a first-in-human, phase 1/2, dose-escalation and selection, pharmacokinetic (PK)/pharmacodynamic (PD), safety, and efficacy study in adult patients with R/R or treatment-naive B-cell malignancies. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the MAH requested one additional year of market protection

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. Alemtuzumab - LEMTRADA (CAP) - PSUSA/00010055/202109

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Bedaquiline - SIRTURO (CAP) - PSUSA/00010074/202109

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Bupivacaine, meloxicam - ZYNRELEF (CAP) - PSUSA/00010880/202109

Applicant: Heron Therapeutics, B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Cabotegravir - VOCABRIA (CAP) - PSUSA/00010900/202109

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Caplacizumab - CABLIVI (CAP) - PSUSA/00010713/202108

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Cholic acid[10] - ORPHACOL (CAP) - PSUSA/00010208/202109

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Crizotinib - XALKORI (CAP) - PSUSA/00010042/202108

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Damoctocog alfa pegol - JIVI (CAP) - PSUSA/00010732/202108

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA (CAP) - PSUSA/00010646/202109

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[10] Oxosteroid-reductase or hydroxy-steroid dehydrogenase deficiency indication(s) only

6.1.10. Darvadstrocel - ALOFISEL (CAP) - PSUSA/00010676/202109

Applicant: Takeda Pharma A/S, ATMP[11]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.11. Deferiprone - FERRIPROX (CAP) - PSUSA/00000940/202108

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Doravirine - PIFELTRO (CAP) - PSUSA/00010729/202108

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

6.1.13. Doravirine, lamivudine, tenofovir disoproxil - DELSTRIGO (CAP) - PSUSA/00010731/202108

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

6.1.14. Dulaglutide - TRULICITY (CAP) - PSUSA/00010311/202109

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Duvelisib - COPIKTRA (CAP) - PSUSA/00010939/202109

Applicant: Secura Bio Limited

PRAC Rapporteur: Željana Margan Koletić

[11] Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Esketamine[12] - SPRAVATO (CAP) - PSUSA/00010825/202109

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Filgotinib - JYSELECA (CAP) - PSUSA/00010879/202109

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Fremanezumab - AJOVY (CAP) - PSUSA/00010758/202109

Applicant: TEVA GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Gilteritinib - XOSPATA (CAP) - PSUSA/00010832/202109

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Human coagulation factor VIII, human von Willebrand factor[13] - VONCENTO (CAP) - PSUSA/00010102/202108

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Centrally authorised product(s) only
[13] Centrally authorised product(s) only

6.1.21. Ibalizumab - TROGARZO (CAP) - PSUSA/00010797/202109

Applicant: Theratechnologies Europe Limited

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Idebenone[14] - RAXONE (CAP) - PSUSA/00010412/202109

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

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/00001742/202108

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Isatuximab - SARCLISA (CAP) - PSUSA/00010851/202109

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Isavuconazole - CRESEMBA (CAP) - PSUSA/00010426/202109

Applicant: Basilea Pharmaceutica Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Lacosamide - LACOSAMIDE UCB (CAP); VIMPAT (CAP) - PSUSA/00001816/202108

Applicant(s): UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

[14] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Linaclotide - CONSTELLA (CAP) - PSUSA/00010025/202108

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Lorlatinib - LORVIQUA (CAP) - PSUSA/00010760/202109

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Loxapine[15] - ADASUVE (CAP) - PSUSA/00010113/202108

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Mecasermin - INCRELEX (CAP) - PSUSA/00001942/202108

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Mepolizumab - NUCALA (CAP) - PSUSA/00010456/202109

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Pre-dispensed inhalation powder only

6.1.32. Meropenem, vaborbactam - VABOREM (CAP) - PSUSA/00010727/202108

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

6.1.33. Naloxegol - MOVENTIG (CAP) - PSUSA/00010317/202109

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Naltrexone, bupropion - MYSIMBA (CAP) - PSUSA/00010366/202109

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Obiltoxaximab - OBILTOXAXIMAB SFL (CAP) - PSUSA/00010885/202109

Applicant: SFL Pharmaceuticals Deutschland GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Pandemic influenza vaccine (H5N1) (whole virion, Vero cell derived, inactivated) - PANDEMIC INFLUENZA VACCINE H5N1 BAXTER (CAP) - PSUSA/00002282/202108

Applicant: Ology Bioservices Ireland Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Pembrolizumab - KEYTRUDA (CAP) - PSUSA/00010403/202109

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

6.1.38. Ponesimod - PONVORY (CAP) - PSUSA/00010940/202109

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Rilpivirine[16] - REKAMBYS (CAP) - PSUSA/00010901/202109

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Sebelipase alfa - KANUMA (CAP) - PSUSA/00010422/202108

Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Solriamfetol - SUNOSI (CAP) - PSUSA/00010831/202109

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Somapacitan - SOGROYA (CAP) - PSUSA/00010920/202108

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[16] Intramuscular use only

6.1.43. Teduglutide - REVESTIVE (CAP) - PSUSA/00009305/202108

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Tildrakizumab - ILUMETRI (CAP) - PSUSA/00010720/202109

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Trabectedin - YONDELIS (CAP) - PSUSA/00003001/202109

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Velmanase alfa - LAMZEDE (CAP) - PSUSA/00010677/202109

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

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. Brinzolamide - AZOPT (CAP); NAP - PSUSA/00000432/202108

Applicants: Novartis Europharm Limited (Azopt), various

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Epoetin alfa - ABSEAMED (CAP), BINOCRIT (CAP), EPOETIN ALFA HEXAL (CAP); NAP - PSUSA/00001237/202108

Applicants: Medice Arzneimittel Pütter GmbH & Co. KG (Abseamed), Sandoz GmbH (Binocrit), Hexal AG (Epoetin alfa Hexal), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Glycopyrronium[17] - SIALANAR (CAP); NAP - PSUSA/00010529/202109

Applicants: Proveca Pharma Limited (Sialanar), various

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Irbesartan - APROVEL (CAP), IRBESARTAN ZENTIVA (CAP), KARVEA (CAP), irbesartan, hydrochlorothiazide - COAPROVEL (CAP), IRBESARTAN HYDROCHLOROTHIAZIDE ZENTIVA (CAP), KARVEZIDE (CAP); NAP - PSUSA/00010601/202108

Applicants: sanofi-aventis groupe (Aprovel, CoAprovel, Karvea, Karvezide), Zentiva, k.s. (Irbesartan Hydrochlorothiazide Zentiva, Irbesartan Zentiva), various

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Mercaptopurine - XALUPRINE (CAP); NAP - PSUSA/00001988/202109

Applicants: Nova Laboratories Ireland Limited (Xaluprine), various

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Trientine - CUFENCE (CAP), CUPRIOR (CAP); NAP - PSUSA/00010637/202109

Applicants: Univar Solutions BV (Cufence), Orphalan (Cuprior), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[17] Treatment of severe sialorrhea (chronic pathological drooling) indication(s) only

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

6.3.1. Aniracetam (NAP) - PSUSA/00010790/202108

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Asparaginase, crisantaspase[18] (NAP) - PSUSA/00003161/202108

Applicant(s): various

PRAC Lead: Roxana Dondera

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Buserelin (NAP) - PSUSA/00000462/202108

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Cetirizine, pseudoephedrine (NAP) - PSUSA/00000629/202108

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Ciclesonide (NAP) - PSUSA/00000742/202108

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[18] Nationally authorised product(s) only

6.3.6. Dermatophagoides pteronyssinus, dermatophagoides farina[19] [20] [21] (NAP) - PSUSA/00010582/202109

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Dexamfetamine (NAP) - PSUSA/00000986/202109

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Esketamine[22] (NAP) - PSUSA/00001266/202108

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Estradiol[23] (NAP) - PSUSA/00010440/202108

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Etonogestrel (NAP) - PSUSA/00001331/202109

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[19] Allergen for therapy
[20] Oromucosal use only
[21] Medicinal product(s) authorised via mutually recognition procedure and decentralised procedure only
[22] Except for centrally authorised product(s)
[23] Except cream, balm, emulsion for application in female genital area

6.3.11. Finasteride (NAP) - PSUSA/00001392/202108

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Gadobenic acid (NAP) - PSUSA/00001500/202108

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Gadobutrol (NAP) - PSUSA/00001502/202108

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Gadopentetic acid (NAP) - PSUSA/00001504/202108

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Gadoteric acid[24] (NAP) - PSUSA/00001506/202108

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Gadoteridol (NAP) - PSUSA/00001507/202108

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

[24] Intravenous (IV) and intravascular formulation(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Gadoxetic acid disodium (NAP) - PSUSA/00001509/202108

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Meropenem (NAP) - PSUSA/00001989/202108

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Modafinil (NAP) - PSUSA/00010242/202108

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Nifuroxazide (NAP) - PSUSA/00002160/202108

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Oxcarbazepine (NAP) - PSUSA/00002235/202108

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Penciclovir (NAP) - PSUSA/00002333/202108

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Pilocarpine[25] (NAP) - PSUSA/00002410/202108

Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Rilmenidine (NAP) - PSUSA/00002643/202108

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Tuberculin purified protein derivative (NAP) - PSUSA/00003063/202109

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/LEG 051.1

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to LEG 051 [cumulative review including all available data of cases of paresis, bone marrow necrosis, deafness, melanoma, pancreatic cancer, squamous cell carcinoma and toxic epidermal necrolysis following the addition of these adverse drug reactions (ADRs) in the US product information at the FDA's request, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000235/202009) adopted in June 2021] as per the request for supplementary information (RSI) adopted in December 2021[26]

Action: For adoption of advice to CHMP

[25] Ophthalmic formulation(s) only
[26] Held 29 November – 02 December 2021

6.4.2. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/LEG 008.2

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to LEG 008.1 [review of cases of rapid correction of hyponatremia and neurological sequelae as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010395/202005) adopted in January 2021] as per the request for supplementary information (RSI) adopted in December 2021[27]

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0031

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 4.4 of the SmPC in order to add new warnings on major adverse cardiac events (MACE) and amend an existing warning on malignancy and venous thromboembolism (VTE) as requested in the conclusions of the last PSUR single assessment (PSUSA) procedure (PSUSA/00010578/202102) adopted in September 2021 and based on interim results from study I4V-MC-B023: a retrospective observational study to compare baricitinib relative to the standard of care. The package leaflet and the RMP (version 13.1) are updated accordingly. In addition, the MAH submitted a proposal for a direct healthcare professional communication (DHPC) and a communication plan

Action: For adoption of PRAC Assessment Report

6.5.2. Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/WS2168/0114; PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/WS2168/0043

Applicant: Upjohn EESV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.4 and 4.8 of the SmPC to reflect new data on suicidal ideation as requested in the outcome of the review assessed in LEG 0054 (Lyrica) and LEG 007 (Pregabalin Pfizer) adopted in April 2021 and requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002511/202001) adopted in September 2020

Action: For adoption of PRAC Assessment Report

[27] Held 29 November - 02 December 2021

6.6. Expedited summary safety reviews[28]

6.6.1. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) (NVX-CoV2373) - NUVAXOVID (CAP MAA) - EMEA/H/C/005808/MEA 014

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: First expedited summary safety report (SSR) for Nuvaxovid (COVID-19 vaccine (recombinant, adjuvanted)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.2. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 011.11

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Twelfth expedited summary safety report (SSR) for Spikevax (elasomeran) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.3. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.12

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Thirteenth expedited summary safety report (SSR) for Comirnaty (tozinameran) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[29]

7.1.1. Evinacumab – EVKEEZA (CAP) - EMEA/H/C/PSP/S/0096.1

Applicant: Regeneron Ireland DAC

PRAC Rapporteur: Annika Folin

Scope: MAH's response to PSP/S/0096 [protocol for a study to evaluate long-term effects of evinacumab treatment in patients with homozygous familial hypercholesterolemia (HoFH), including safety outcomes in patients with HoFH who are ≥12 years old, frequency and

[28] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

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

outcomes of pregnancy in female patients with HoFH, atherosclerosis process over time in patients with HoFH who undergo cardiovascular imaging and frequency of cardiovascular imaging of patients with HoFH] as per the request for supplementary information (RSI) adopted in December 2021[30]

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

7.1.2. Fenfluramine – FINTEPLA (CAP) - EMEA/H/C/PSP/S/0093.2

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0093.1 [protocol for an observational registry to provide data on long-term safety of fenfluramine in routine practice, with a focus on characterising and quantifying the important potential risks of valvular heart disease (VHD) and pulmonary arterial hypertension (PAH) (primary objective), and growth retardation (secondary objective). In addition, data on the frequency of echocardiographic monitoring contribute to assess the effectiveness of risk minimisation measures] as per the request for supplementary information (RSI) adopted in October 2021[31]

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

7.1.3. Valproate[32] (NAP) - EMEA/H/N/PSP/J/0094.2

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0094.1 [protocol for a joint retrospective study of multiple European data sources characterising neurodevelopmental disorders in children exposed in utero to valproate and/or other antiepileptic drugs with long-term follow-up] as per the request for supplementary information (RSI) adopted in November 2021[33]

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[34]

7.2.1. Diroximel fumarate - VUMERITY (CAP) - EMEA/H/C/005437/MEA 001

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Protocol for study 272MS401: Vumerity (diroximel fumarate) prospective multiple sclerosis (MS) pregnancy exposure registry

Action: For adoption of advice to CHMP

[30] Held 29 November – 02 December 2021
[31] Held 27-30 September 2021
[32] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium
[33] Held 25-28 October 2021
[34] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

7.2.2. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 034.2

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: MAH's response to MEA 034.1 [protocol for a study monitoring the safety of Spikevax (COVID-19 vaccine) in pregnancy: an observational study using routinely collected health data in five European countries] as per the request for supplementary information (RSI) adopted in September 2021[35] together with a statistical analysis plan (SAP)

Action: For adoption of advice to CHMP

7.2.3. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 005.2

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 005.1 [protocol for study ZX008-2102: a drug utilisation study (DUS) in Europe to describe fenfluramine use in routine clinical practice [final report expected in August 2025] (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in October 2021[36]

Action: For adoption of advice to CHMP

7.2.4. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 006.1

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 006 [protocol for study ZX008-2104: a European study of the effectiveness of risk minimisation measures for fenfluramine in Dravet syndrome] as per the request for supplementary information (RSI) adopted in October 2021[37]

Action: For adoption of advice to CHMP

7.2.5. Netarsudil - RHOKIINSA (CAP) - EMEA/H/C/004583/MEA 001.3

Applicant: Santen Oy

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 001.2 [protocol for study AR-13324-OBS02: a non-interventional, observational cohort study of 2-year of treatment with Rhokiinsa (netarsudil) compared with non-Rhokiinsa (netarsudil) ocular hypotensive therapy in patients with elevated intraocular pressure due to primary open angle glaucoma or ocular hypertension] as per the request for supplementary information (RSI) adopted in September 2021[38]

Action: For adoption of advice to CHMP

[35] Held 30 August – 02 September 2021
[36] Held 27-30 September 2021
[37] Held 27-30 September 2021
[38] Held 30 August – 02 September 2021

7.2.6. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/MEA 003

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Protocol for study A4250-019 (listed as a category 3 study in the RMP): registry-based safety study in order to collect safety data on hepatotoxicity, diarrhoea, fat-soluble vitamins and fat-soluble nutrients in patients treated with odevixibat [final study report expected in December 2026]

Action: For adoption of advice to CHMP

7.2.7. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/MEA 004

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Protocol for study A4250-020 (listed as a category 3 study in the RMP): a disease registry to document the natural history of the disease, treatment efficacy, safety, including long-term outcomes, pregnancy, breastfeeding and newborns in patients with progressive familial intrahepatic cholestasis (PFIC)

Action: For adoption of advice to CHMP

7.2.8. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 002.4

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002.3 [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] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CHMP

7.2.9. Somapacitan - SOGROYA (CAP) - EMEA/H/C/005030/MEA 002.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002.1 [protocol for study NN8640-4515: a multinational, multicentre, prospective, open label, single-arm, observational, non-interventional PASS to investigate long-term safety of somapacitan in adults with growth hormone deficiency (AGHD) under normal clinical practice conditions (from initial marketing authorisation/opinion)] as per the request for supplementary information (RSI) adopted in January 2022

Action: For adoption of advice to CHMP

7.2.10. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 014.5

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 014.4 [protocol for study A3921321: a drug utilisation study (DUS) on the utilisation and prescribing patterns of Xeljanz (tofacitinib) in two European countries using administrative claims databases and national registries for assessment, as requested in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1485) finalised in November 2019] as per the request for supplementary information (RSI) adopted in December 2021[39]

Action: For adoption of advice to CHMP

7.2.11. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.4

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Amendment to a protocol previously agreed in April 2021 [MEA 011] for study C4591010: a post-approval active surveillance safety study to monitor real-world safety of the Pfizer-BioNTech COVID-19 vaccine (Comirnaty) in the EU

Action: For adoption of advice to CHMP

7.2.12. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 053

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for study CNTO1275PSO4005: a Nordic database initiative for exposure to ustekinumab - a review and analysis of major adverse cardiovascular events (MACE) from the Swedish and Danish national registry systems

Action: For adoption of advice to CHMP

7.2.13. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 054

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for study PCSIMM004697: an observational longitudinal PASS of Stelara (ustekinumab) in the treatment of psoriasis and psoriatic arthritis - analysis of major adverse cardiovascular events (MACE) using Swedish national health registers

Action: For adoption of advice to CHMP

[39] Held 29 November – 02 December 2021

7.3. Results of PASS imposed in the marketing authorisation(s)[40]

7.3.1. Dexketoprofen, tramadol (NAP) - EMEA/H/N/PSR/S/0035

Applicant: Menarini International Operations Luxembourg S.A. (Dextradol, Enanplus, Skudexa, Takudex)

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to PSR/S/0035 [results of a drug utilisation study (DUS) and PASS on tramadol-dexketoprofen (DKP-TRAM) fixed combination to evaluate pattern of prescriptions of DKP-TRAM and assess the risk of adverse events (AE) (e.g. nausea, vomiting, diarrhoea, vertigo) in DKP-TRAM vs. tramadol monotherapy (including tramadol-paracetamol combinations) users, with a special focus on patients 75 years old and over] as per the request for supplementary information (RSI) adopted in November 2021[41]

Action: For adoption of recommendation to CMDh (or request for supplementary information (RSI))

7.4. Results of PASS non-imposed in the marketing authorisation(s)[42]

7.4.1. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/II/0039

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final study report (CSR) from the UK Clinical Practice Research Database (CPRD) (listed as a category 3 study in the RMP): an observational study to assess the long-term data of apremilast in patients with psoriasis and psoriatic arthritis. The RMP (version 14.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/II/0058/G, Orphan

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) submission of the final study report of the DEFIFrance registry (listed as a category 3 study in the RMP): a national, post-registration observational study of the long-term safety and health outcome of patients treated with Defitelio (defibrotide), including patients with severe hepatic veno-occlusive disease (VOD) after hematopoietic stem-cell transplantation (HSCT) (in fulfilment of LEG 011.3). The RMP (version 9.2) is updated accordingly; 2) submission of an updated RMP (version 9.2) in order to remove reproductive toxicity as a potential risk

Action: For adoption of PRAC Assessment Report

[40] In accordance with Article 107p-q of Directive 2001/83/EC
[41] Held 25-28 October 2021
[42] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

7.4.3. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/WS2223/0066/G; empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/WS2223/0043/G; empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/WS2223/0062/G

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) submission of the final report from PASS 1245.146 (listed as a category 3 study in the RMP): a 5-year enhanced pharmacovigilance surveillance initiative to survey and characterise spontaneous occurrence and experience of ketoacidotic events in patients treated with empagliflozin-containing products. The RMP is updated accordingly; 2) submission of updated RMPs for Jardiance (version 18.0), for Glyxambi (version 7.0) and for Synjardy (version 12.0) in order to remove bone fracture, classified as an important potential risk and pregnancy/breast-feeding as missing information

Action: For adoption of PRAC Assessment Report

7.4.4. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - CERVARIX (CAP) - EMEA/H/C/000721/II/0114

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study EPI-HPV-048 (listed as a category 3 study in the RMP.): a surveillance study part of a two-phase national human papillomavirus vaccine (HPV) surveillance programme initiated in the UK by the Health Protection Agency in order to evaluate the impact of HPV vaccination on HPV type replacement and to assess the prevalence of type-specific HPV deoxyribonucleic acid (DNA) in young women in England since HPV immunisation using Cervarix (human papillomavirus vaccine) was introduced (in fulfilment of MEA 094). In addition, the submission includes the protocol for study EPI-HPV-099: an observational, retrospective database PASS to assess trends and changes over time in incidence of anal cancer and feasibility for a case-control study in European countries that introduced Cervarix (human papillomavirus vaccine) in their National Immunisation Programmes (NIP) in order to address the safety concern of 'impact and effectiveness against anal lesions and cancer'. The RMP (version 25) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. Sirolimus - RAPAMUNE (CAP) - EMEA/H/C/000273/II/0184

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from non-interventional study B1741224 (listed as a category 3 study in the RMP): a population-based cohort study to monitor the safety and effectiveness of sirolimus in patients with sporadic lymphangioleiomyomatosis (S-LAM)

Action: For adoption of PRAC Assessment Report

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

7.5.1. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 002.4

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Fifth annual interim report from an established nationwide register: British Society for Rheumatology Rheumatoid Arthritis Register (BSRBR-RA) for patients with rheumatological disorders treated with biologic agents, designed as a national prospective study whose primary purpose is to assess long-term toxicity from the use of these agents in routine practice [final report expected in 2027]

Action: For adoption of advice to CHMP

7.5.2. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 003.4

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Fifth annual interim report from an established nationwide register: Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) for patients with rheumatological disorders treated with biologic agents, designed as a national prospective study whose primary purpose is to assess long-term toxicity from the use of these agents in routine practice [final report expected in 2027]

Action: For adoption of advice to CHMP

7.5.3. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 004.4

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Fifth annual interim report for study from the Anti-Rheumatic Treatment in Sweden (ARTIS) register: a national prospective, observational, uncontrolled cohort study evaluating the risk of selected adverse events (AEs) in rheumatoid arthritis (RA), juvenile idiopathic arthritis, and other rheumatic disease patients treated with etanercept [final report expected in 2027]

Action: For adoption of advice to CHMP

7.5.4. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 005.4

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Fifth annual interim report for study from the British Association of Dermatologists Biologic Interventions Register (BADBIR): a national prospective, observational cohort study of patients with psoriasis, which compares patients treated with biological interventions to a

control group not exposed to biologicals [final report expected in 2027]

Action: For adoption of advice to CHMP

7.5.5. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 009.1

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 009 [interim report for the Chronisch Entzündliche Darmerkrankungen, ein Unabhängiges Register (CEDUR) to describe the long-term effectiveness of treatment with inflammatory bowel disease (IBD) therapies such as drug survival, effectiveness, side effects of treatment combination, and disease activity achieved] as per the request for supplementary information (RSI) adopted in November 2021[43]

Action: For adoption of advice to CHMP

7.5.6. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 010.1

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 010 [interim report for the Czech Register of inflammatory bowel disease (IBD) Patients on Biological Therapy (CREDIT) to monitor effectiveness of total population of IBD patients on biological medication in the Czech Republic and regular analytical evaluation of the effectiveness] as per the request for supplementary information (RSI) adopted in November 2021[44]

Action: For adoption of advice to CHMP

7.5.7. Octocog alfa - KOGENATE BAYER (CAP) - EMEA/H/C/000275/MEA 086.10

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Twelfth annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry [final clinical study report (CSR) expected in December 2021]

Action: For adoption of advice to CHMP

7.5.8. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 004.4

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Twelfth annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events

[43] Held 25-28 October 2021
[44] Held 25-28 October 2021

(AEs) of special interest in the EUHASS registry [final clinical study report (CSR) expected in December 2021]

Action: For adoption of advice to CHMP

7.5.9. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 001.7

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual progress report for study TEG4001: a prospective, non-interventional, long-term, multinational cohort safety study of patients with hereditary transthyretin amyloidosis with polyneuropathy (hATTR-PN)

Action: For adoption of advice to CHMP

7.5.10. Rurioctocog alfa pegol - ADYNOVI (CAP) - EMEA/H/C/004195/ANX 002.1

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study SHP660-403: a PASS to investigate the potential effects of PEG accumulation in the choroid plexus of the brain and other tissues/organs, [final study report expected in Q1 2029] (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CHMP

7.5.11. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/ANX 003.7

Applicant: Novartis Europharm Limited, ATMP[45]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Fourth semi-annual report for study CCTL019B2401: a non-interventional PASS to further characterise the safety, including long-term safety, of Kymriah (tisagenlecleucel) based on data from a disease registry in acute lymphoblastic leukaemia (ALL) and diffuse large B-cell lymphoma (DLBCL) patients (European Society for Blood and Marrow Transplant Society Registry (EBMT) data only)

Action: For adoption of advice to CAT and CHMP

7.5.12. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.3

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study C4591012: clinical study to assess the occurrence of safety events of interest, including severe or atypical COVID-19 in real-world use of COVID-19 mRNA vaccine [final clinical study report (CSR) expected in December 2023]

Action: For adoption of advice to CHMP

[45] Advanced therapy medicinal product

7.6. Others

7.6.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 006.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Statistical analysis plan (SAP) for study COVID-19 vaccines International Pregnancy Exposure Registry (C-VIPER) (listed as a category 3 study in the RMP): a pregnancy registry of women exposed to Vaxzevria (AZD1222 – COVID-19 vaccine) immediately before or during pregnancy (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CHMP

7.6.2. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 004.5

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of a statistical analysis plan (SAP) for study mRNA-1273-P904 (study 1) (listed as a category 3 study in the RMP): a post-authorisation active surveillance safety study using secondary data to monitor real-world safety of Spikevax (COVID-19 mRNA-1273 vaccine) in Europe - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals in European populations and electronic database assessment of use in pregnant women [final clinical study report (CSR) expected in December 2023]

Action: For adoption of advice to CHMP

7.6.3. Icatibant - FIRAZYR (CAP) - EMEA/H/C/000899/MEA 034

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Proposal for discontinuation of icatibant outcome survey (IOS): a prospective, international, observational open-ended disease registry designed to document over time the routine clinical outcomes of adult and paediatric patients with hereditary angioedema (HAE; HAE types I and II and HAE with normal C1-esterase inhibitor), angiotensin converting enzyme inhibitor (ACE-I)-induced angioedema, non-histaminergic idiopathic angioedema, and acquired angioedema; and notification of change to the legal entity sponsoring the study

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/S/0041 (without RMP)

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/S/0057 (with RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0044 (without RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Tagraxofusp - ELZONRIS (CAP) - EMEA/H/C/005031/S/0012 (without RMP)

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/R/0067 (without RMP)

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Belantamab mafodotin - BLENREP (CAP) - EMEA/H/C/004935/R/0010 (without RMP)

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Bulevirtide - HEPCLUDEX (CAP) - EMEA/H/C/004854/R/0013 (without RMP)

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/R/0029 (without RMP)

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.5. Idecabtagene vicleucel - ABECMA (CAP) - EMEA/H/C/004662/R/0014 (with RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP[46]

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

[46] Advanced therapy medicinal product

8.2.6. Imlifidase - IDEFIRIX (CAP) - EMEA/H/C/004849/R/0007 (without RMP)

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.7. Pretomanid - DOVPRELA (CAP) - EMEA/H/C/005167/R/0010 (without RMP)

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Copper (^{64}Cu) chloride - CUPRYMINA (CAP) - EMEA/H/C/002136/R/0023 (without RMP)

Applicant: A.C.O.M. - Advanced Center Oncology Macerata - S.R.L.

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/R/0053 (without RMP)

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Entecavir - ENTECAVIR ACCORD (CAP) - EMEA/H/C/004458/R/0011 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Entecavir - ENTECAVIR MYLAN (CAP) - EMEA/H/C/004377/R/0008 (with RMP)

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Lacosamide - LACOSAMIDE ACCORD (CAP) - EMEA/H/C/004443/R/0015 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Nitisinone - NITISINONE MDK (CAP) - EMEA/H/C/004281/R/0013 (without RMP)

Applicant: MendeliKABS Europe Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Telotristat ethyl - XERMELO (CAP) - EMEA/H/C/003937/R/0032 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

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 CHMP or EMA

10.1. Safety related variations of the marketing authorisation

10.1.1. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/II/0029

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: PRAC consultation in a variation to update sections 4.4, 4.8 and 5.1 of the SmPC based on final results from study CO-338-043 (ARIEL4) (listed as a specific obligation in Annex II): a phase 3, multicentre, open-label, randomised study evaluating the efficacy and safety of rucaparib versus chemotherapy for treatment of relapsed ovarian cancer. The package leaflet and the RMP (version 6.1) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes and bring the product information in line with the latest bring the product information in line with the latest quality review of documents (QRD) template (version 10.2 Rev.1)

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Ibuprofen (NAP) - DE/H/0392/II/032/G

Applicant: Johnson & Johnson GmbH (Dolormin für Kinder Ibuprofensaft 20 mg/mL)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a grouped type II variations (DE/H/0392/II/032/G) on the use

of ibuprofen during pregnancy, on request of Germany

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. Vote by proxy

None

12.1.3. Relaunch of face-to-face scientific Committee meetings - pilot

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

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

12.8.1. Marketing authorisation applications (MAA) forecast for 2022 – planning update dated Q1 2022

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.18.3. Direct healthcare professional communication (DHPC) review process - proposal for improvement

Action: For discussion

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

12.20.1. Strategy on measuring the impact of pharmacovigilance activities revision 2 – PRAC interest group (IG) Impact

Action: For adoption

12.20.2. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact – revision of the process for prioritisation and follow-up of impact research

Action: For adoption

12.20.3. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact – pilot for enhancing PRAC stakeholder engagement

PRAC lead: Daniel Morales

Action: For adoption

12.21. Others

12.21.1. EMA-funded study on thrombosis and thrombocytopenia syndrome (TTS) after vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – study results

Action: For discussion

12.21.2. EMA-funded study on early safety monitoring of coronavirus 2019 (COVID-19) vaccines in EU Member States – study results

Action: For discussion

12.21.3. Questions and answers (Q&A) document on 'complex clinical trials' - draft

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:
https://www.ema.europa.eu/en