07 February 2022
EMA/PRAC/76191/2022
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 07-10 February 2022

Chair: Sabine Straus – Vice-Chair: Martin Huber

07 February 2022, 10:30 – 19:30, via teleconference

08 February 2022, 08:30 – 19:30, via teleconference

09 February 2022, 08:30 – 19:30, via teleconference

10 February 2022, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

24 February 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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 07-10 February 2022. See February 2022 PRAC minutes (to be published post March 2022 PRAC meeting).

1.2. Agenda of the meeting on 07-10 February 2022

Action: For adoption

1.3. Minutes of the previous meeting on 10-13 January 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

3.1.1. Janus kinase (JAK) inhibitors[1]: abrocitinib - CIBINQO (CAP); baricitinib - OLUMIANT (CAP); filgotinib - JYSELECA

[1] Indicated for the treatment of inflammatory disorders

(CAP); tofacitinib - XELJANZ (CAP); upadacitinib - RINVOQ (CAP) – EMEA/H/A-20/1517

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Rinvoq), Eli Lilly Nederland B.V. (Olumiant), Galapagos N.V. (Jyseleca), Pfizer Europe MA EEIG (Cibinqo, Xeljanz)

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

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

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

3.2. Ongoing procedures

3.2.1. Chlormadinone (NAP); chlormadinone, ethinylestradiol (NAP); nomegestrol (NAP); nomegestrol, estradiol – ZOELY (CAP), NAP - EMEA/H/A-31/1510

Applicant(s): Theramex Ireland Limited (Zoely), various

PRAC Rapporteur: Martin Huber; PRAC Co-rapporteur: Željana Margan Koletić

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

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

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

None

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

4.2. New signals detected from other sources

4.2.1. Coronavirus (COVID-19) mRNA[4] vaccine (nucleoside-modified) - SPIKEVAX (CAP)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: To be appointed

Scope: Signal of amenorrhea

Action: For adoption of PRAC recommendation

EPITT 19781 – New signal

Lead Member State(s): DE, DK

4.2.2. Coronavirus (COVID-19) mRNA[5] vaccine (nucleoside-modified) - SPIKEVAX (CAP)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: To be appointed

Scope: Signal of heavy menstrual bleeding

Action: For adoption of PRAC recommendation

EPITT 19780 – New signal

Lead Member State(s): DE, DK

4.2.3. Tozinameran - COMIRNATY (CAP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: To be appointed

Scope: Signal of amenorrhea

Action: For adoption of PRAC recommendation

EPITT 19784 – New signal

Lead Member State(s): NL, NO

4.2.4. Tozinameran - COMIRNATY (CAP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: To be appointed

Scope: Signal of heavy menstrual bleeding

Action: For adoption of PRAC recommendation

EPITT 19783 – New signal

Lead Member State(s): NL, NO

[4] Messenger ribonucleic acid
[5] Messenger ribonucleic acid

4.3. Signals follow-up and prioritisation

4.3.1. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/SDA/015

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Signal of erythema multiforme

Action: For adoption of PRAC recommendation

EPITT 19734 – Follow-up to October 2021

4.3.2. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/SDA/012

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Signal of non-overt disseminated intravascular coagulation (DIC)

Action: For adoption of PRAC recommendation

EPITT 19711 – Follow-up to September 2021

4.3.3. Sorafenib - NEXAVAR (CAP) - EMEA/H/C/000690/SDA/041

Applicant: Bayer AG

PRAC Rapporteur: Annika Folin

Scope: Signal of tumour lysis syndrome (TLS)

Action: For adoption of PRAC recommendation

EPITT 19733 – Follow-up to October 2021

4.3.4. Tocilizumab – ROACTEMRA (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of drug reaction with eosinophilia and systemic symptoms

Action: For adoption of PRAC recommendation

EPITT 19360 – Follow-up to September 2019

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Coronavirus (COVID-19) mRNA[6] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0028

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 2.1) to include myocarditis and pericarditis in the list of the safety concerns as an important identified risk, as requested in the outcome of the signal procedure on myocarditis and pericarditis (EPITT 19713) adopted in July 2021 (SDA 033)

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Bevacizumab - EMEA/H/C/005574

Scope: Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer; first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer; first line treatment of patients with advanced and/or metastatic renal cell cancer

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. Dabigatran etexilate - EMEA/H/C/005639

Scope: Prevention of venous thromboembolic events

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

[6] Messenger ribonucleic acid

5.1.4. Fosdenopterin - EMEA/H/C/005378, Orphan

Applicant: Comharsa Life Sciences Ltd

Scope (accelerated assessment): Treatment of molybdenum cofactor deficiency type A

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

5.1.5. Insulin human - EMEA/H/W/005779

Scope: Treatment of diabetes mellitus

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

5.1.6. Insulin human - EMEA/H/W/005780

Scope: Treatment of diabetes mellitus

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

5.1.7. Molnupiravir – LAGEVRIO (CAP MAA) - 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. Olipudase alfa - EMEA/H/C/004850, PRIME, Orphan

Applicant: Genzyme Europe BV

Scope (accelerated assessment): Treatment of non-central nervous system (CNS) manifestations of acid sphingomyelinase deficiency (ASMD) in paediatric and adult patients with type A/B or type B

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

5.1.9. Pirfenidone - EMEA/H/C/005873

Scope: Treatment of mild to moderate idiopathic pulmonary fibrosis (IPF)

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

5.1.10. Ranibizumab - EMEA/H/C/005610

Scope: Treatment of neovascular age-related macular degeneration in adults

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. Alogliptin - VIPIDIA (CAP) - EMEA/H/C/002182/WS2191/0029; alogliptin, metformin - VIPDOMET (CAP) - EMEA/H/C/002654/WS2191/0036; alogliptin, pioglitazone - INCRESYNC (CAP) - EMEA/H/C/002178/WS2191/0040

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 11) in order to consolidate it within a single RMP for Vipidia (alogliptin), Vipdomet (alogliptin/metformin) and Incresync (alogliptin/pioglitazone) as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010061/202104) finalised in November 2021. The consolidated RMP is also updated in line with revision 2 of GVP module V on 'Risk management systems' and the targeted follow up questionnaires (FUQ) of severe hypersensitivity and skin reactions, pancreatitis, hepatic events and follow up gastrointestinal events and infections is removed. Finally, the removal of the inverted black triangle as agreed other procedures is reflected in the RMP

Action: For adoption of PRAC Assessment Report

5.2.2. Coronavirus (COVID-19) mRNA[7] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0022

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 2.0) to include clinical safety data from study mRNA-1273 P203 (NCT04649151): a phase 2/3, randomised, observer-blind, placebo-controlled study evaluating the safety, reactogenicity and effectiveness of the mRNA-1273 vaccine in healthy adolescents aged ≥ 12 to < 18 years

Action: For adoption of PRAC Assessment Report

5.2.3. Nintedanib - VARGATEF (CAP) - EMEA/H/C/002569/II/0044

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Georgia Gkegka

Scope: Submission of an updated RMP (version 10.0) in order to remove safety concerns that were classified as important identified risks, important potential risks and missing information, based on cumulative post-marketing experience. The MAH also proposed an update of the anatomical therapeutic chemical (ATC) code, an update of post-marketing exposure, the removal of adverse event follow-up forms and an update of search strategies

Action: For adoption of PRAC Assessment Report

5.2.4. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - FOCLIVIA (CAP) - EMEA/H/C/001208/WS2151/0068; prepandemic influenza vaccine

[7] Messenger ribonucleic acid

(H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - EMEA/H/C/002094/WS2151/0071

Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 3.9) in order to align safety concerns of Aflunov (prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted)) and Foclivia (pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted)) and to reclassify some potential risks in line with revision 2 of GVP module V on 'Risk management systems'. In addition, reference to adverse drug reaction follow-up forms for routine pharmacovigilance activity are removed

Action: For adoption of PRAC Assessment Report

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

5.3.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/X/0009/G

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form, film-coated tablet; 2) change of the anatomical therapeutic chemical (ATC) code for acalabrutinib from L01XE51 to L01EL02. The RMP (version 4.1) is updated accordingly

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

5.3.2. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0077/G

Applicant: Bayer AG

PRAC Rapporteur: Nathalie Gault

Scope: Grouped applications consisting of: 1) extension of indication to include as a paediatric indication retinopathy of prematurity (ROP). As a consequence, sections 2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 32.1) are updated in accordance. Separate package leaflet is proposed for the guardians of preterm babies; 2) addition of a stand-alone paediatric dosing device, which will be CE marked and cross-labelled to the EU product information

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

5.3.3. Apalutamide - ERLEADA (CAP) - EMEA/H/C/004452/II/0017

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from study TOX11338 (in completion of MEA 006): a 2-year study to better

characterize the carcinogenic potential of JNJ-56021927-AAA (apalutamide) by oral gavage in rats. The RMP (version 4.1) is updated accordingly. In addition, the MAH took the opportunity to include general information in the RMP regarding study TITAN (PCR3002): a phase 3 randomized, placebo-controlled, double-blind study of apalutamide plus androgen deprivation therapy (ADT) versus ADT in subjects with metastatic hormone-sensitive prostate cancer (mHSPC)

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

5.3.4. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0042, Orphan

Applicant: Kite Pharma EU B.V., ATMP[8]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension of indication to include the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after three or more lines of systemic therapy. As a consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the package leaflet are updated. The RMP (version 5.1) is updated in accordance. In addition, the applicant took the opportunity to make minor editorial corrections throughout the SmPC and package leaflet to align with the latest quality review of documents (QRD) template (version 10.2)

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

5.3.5. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0046, Orphan

Applicant: Kite Pharma EU B.V., ATMP[9]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension of indication to include treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL). 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 5.3) are updated in accordance. In addition, the MAH took the opportunity to update the product information with minor editorial changes

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

5.3.6. Baloxavir marboxil - XOFLUZA (CAP) - EMEA/H/C/004974/X/0003/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Grouped applications consisting of: 1) extension application to add a new strength of 80 mg; 2) addition of a new pack size of 1 tablet for 40 mg strength. The RMP (version 1.2) is updated in accordance. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2) to update the local

[8] Advanced therapy medicinal product
[9] Advanced therapy medicinal product

representatives with 'United Kingdom (Northern Ireland)'

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

5.3.7. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0010

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of visual impairment due to diabetic macular oedema (DME). 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 in accordance

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

5.3.8. Buprenorphine - BUVIDAL (CAP) - EMEA/H/C/004651/II/0017

Applicant: Camurus AB

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension of indication to include treatment of moderate to severe chronic pain in patients with opioid dependence. As a consequence, sections 4.1, 4.2, 4.5, 5.1 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 2.1) are updated accordingly

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

5.3.9. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/II/0023

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include monotherapy treatment of adults and adolescent patients aged 12 years and older, with locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory or not eligible to radioactive iodine (RAI) who have progressed during or after prior systemic therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 6.0) are updated in accordance

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

5.3.10. Cariprazine - REAGILA (CAP) - EMEA/H/C/002770/II/0023

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.4, 4.5, 4.6 and 5.2 of the SmPC in order to update pharmacokinetic information based on final results from RGH-188-302 (CAROLA) study (listed as a category 3 study in the RMP): an open-label, single-arm, fixed-sequence, phase 1 trial in female schizophrenia patients to investigate the effect of multiple-dose administration of cariprazine on the pharmacokinetics of a combined oral contraceptive

containing ethinylestradiol and levonorgestrel. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and the package leaflet

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

5.3.11. Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/II/0026

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include monotherapy treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated in accordance

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

5.3.12. Coronavirus (COVID-19) mRNA[10] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0041

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Extension of indication to include use in children of 6-11 years of age based on data from study mRNA-1273-P204: an ongoing phase 2/3, 2-part, open-label, dose-escalation, age de-escalation and subsequent randomised, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 1.3) are updated in accordance

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

5.3.13. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0072

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension of indication to include treatment of paediatric patients aged ≥ 6 to < 18 years with relapsed or refractory systemic anaplastic lymphoma kinase (ALK)-positive anaplastic large cell lymphoma (ALCL) and with unresectable, recurrent, or refractory ALK-positive inflammatory myofibroblastic tumour (IMT) based on the results from: 1) study ADVL0912: a phase 1/2 study of crizotinib, an oral small molecule inhibitor of ALK and C-Met, in children with relapsed/refractory solid tumours and anaplastic large cell lymphoma; 2) study A8081013: a phase 1b open-label study of the safety and clinical activity of crizotinib in tumours with genetic events involving the ALK gene locus. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 8.0) are updated in accordance. In addition, the MAH took the opportunity

[10] Messenger ribonucleic acid

to update the anatomical therapeutic chemical (ATC) code for crizotinib. Moreover, the MAH took the opportunity to implement a minor change in the list of local representatives in the package leaflet

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

5.3.14. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0093

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to change the posology recommendation for paediatric population and add a new warning on hypercalcaemia in paediatric patients with osteogenesis imperfecta (OI) following an urgent safety measure regarding the risk of hypercalcaemia reported very commonly in ongoing clinical trials in paediatric patients with OI treated with denosumab. The package leaflet and the RMP (version 29.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to implement minor editorial changes in the labelling

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

5.3.15. Doravirine - PIFELTRO (CAP) - EMEA/H/C/004747/WS2065/0019; doravirine, lamivudine, tenofovir disoproxil - DELSTRIGO (CAP) - EMEA/H/C/004746/WS2065/0026

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to extend the indication to the paediatric population weighing at least 35 kg. 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 2.1) are updated in accordance. In addition, the MAH took the opportunity to make minor editorial corrections and to update the list of local representatives in the package leaflet

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

5.3.16. Eribulin - HALAVEN (CAP) - EMEA/H/C/002084/II/0060

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to update efficacy and pharmacokinetic information based on results in the paediatric population (6 months to <18 years) from: 1) study E7389-A001-113: A phase 1 study of eribulin mesylate, a novel microtubule targeting chemotherapeutic agent in children with refractory or recurrent solid tumours, including lymphomas; 2) study E7389-G000-223: a phase 2, multicentre, open-label study to assess safety and preliminary activity of eribulin mesylate in paediatric subjects with relapsed/refractory rhabdomyosarcoma (RMS), non-rhabdomyosarcoma soft tissue sarcoma (NRSTS) and Ewing sarcoma (EWS); 3) study E7389-G000-213: a phase 1/2 single-arm study evaluating the safety and efficacy of eribulin mesilate in combination with

irinotecan in children with refractory or recurrent solid tumours. The package leaflet and the RMP (version 6.0) are updated accordingly

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

5.3.17. Gilteritinib - XOSPATA (CAP) - EMEA/H/C/004752/II/0007, Orphan

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the report of an integrated analysis to demonstrate the safety of long term treatment with gilteritinib when all patients enrolled in studies 2215-CL-0101, 2215-CL-0102 and 2215-CL-0301 have completed at least 3 years of treatment with gilteritinib or have withdrawn prior to completing at least 3 years of treatment. The studies refer to: 1) study 2215-CL-0101: a phase 1/2 open-label, dose escalation study investigating the safety, tolerability, pharmacokinetics, and pharmacodynamics of ASP2215 (gilteritinib) in patients with relapsed or refractory acute myeloid leukaemia (AML); 2) study 2215-CL-0102: a phase 1 open-label, dose escalation study investigating the safety, tolerability, pharmacokinetics, and pharmacodynamics of ASP2215 in Japanese patients with relapsed or refractory AML; 3) study 2215-CL-0301: a phase 3 open-label, multicentre, randomized study of ASP2215 versus salvage chemotherapy in patients with relapsed or refractory AML with FMS-like tyrosine kinase 3 (FLT3) mutation. The RMP (version 2.0) is updated in order to address the missing information regarding the safety of Xospata (gilteritinib)

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

5.3.18. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2113/0090; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2113/0108;

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) for Opdivo (nivolumab) in combination with Yervoy (ipilimumab). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 24.0 for Opdivo and version 33.0 for Yervoy) are updated in accordance

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

5.3.19. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2153/0093; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2153/0111;

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC based on final results from study CA209908: a phase 1b/2 clinical trial of nivolumab monotherapy and nivolumab in combination with ipilimumab in paediatric subjects with high grade primary central nervous system (CNS) malignancies. The RMP (version 22.3 for Opdivo) is updated in accordance

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

5.3.20. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0017/G, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 5.3 of the SmPC in order to update the non-clinical information based on final results from study VX-445-TX-015: a 2-year oral carcinogenicity study in rats evaluating the carcinogenic potential of up to 10 mg/kg/day of elexacaftor. The RMP (version 6.0) is updated accordingly; 2) submission of the final report for study VX-661-TX-038: a tezacaftor juvenile toxicity study

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

5.3.21. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/II/0046

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an alternative study: an evaluation of the effect of lomitapide treatment on major adverse cardiovascular events (MACE) in patients with homozygous familial hypercholesterolemia (LILITH) to the currently agreed protocol for study on the effects of lomitapide on carotid and aortic atherosclerosis in patients treated with lomitapide in usual care (CAPTURE) in order to propose an evaluation of the effect of lomitapide treatment on MACE in patients with homozygous familial hypercholesterolemia. As a consequence, Annex II-D and the RMP (version 6.4) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.2)

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

5.3.22. Lumasiran - OXLUMO (CAP) - EMEA/H/C/005040/II/0008, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to clarify administration instructions, remove an existing warning on metabolic acidosis in patients with severe or end stage renal impairment, update the description of adverse reactions injection site reactions, abdominal pain and immunogenicity, update efficacy and pharmacokinetic information based on: 1) interim results from study ALN-GO1-005 (ILLUMINATE-C) (listed as a category 3 study in the RMP): a single arm study to evaluate efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in patients with advanced primary hyperoxaluria type 1 (PH1); 2) available long-term efficacy and safety data from ongoing studies: study ALN-GO1-003 (ILLUMINATE-A): a phase 3 randomized, double-blind, placebo-controlled study with an extended dosing period to evaluate the efficacy and safety of lumasiran in children and adults with PH1 and study ALN-GO1-004 (ILLUMINATE-B): an open-label study to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in infants and young children with primary PH1; 3) study ALN-GO1-002: a phase 2, multicentre, open-label, extension study to evaluate the long-term administration of ALN-GO1 (lumasiran) in patients with PH. 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

5.3.23. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/X/0042

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension application to introduce a new strength of 40 mg for Nucala (mepolizumab) solution for injection in a pre-filled syringe for subcutaneous use to be used in children aged 6 to 11 years. The RMP (version 8.0) is updated accordingly

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

5.3.24. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/II/0027

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 5.1 of the SmPC in order to update the pharmacokinetic information with descriptive diarrhoea characteristics based on final results from study PUMA-NER-6201 (CONTROL) (listed as a category 3 study in the RMP):an open-label study to characterize the incidence and severity of diarrhoea in patients with early stage human epidermal growth factor receptor-2+ (HER2+) breast cancer treated with neratinib and loperamide. The RMP (version 2.1) is updated accordingly. In addition, the MAH took the opportunity to introduce editorial updates in the product information

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

5.3.25. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/II/0033, Orphan

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning and add myelodysplastic syndrome (MDS)/acute myeloid leukaemia (AML) to the list of adverse drug reactions (ADRs) with a frequency common, and update of section 5.1 based on final results from study 213356 (NOVA): a phase 3 randomized double-blind trial of maintenance with niraparib versus placebo in patients with platinum sensitive ovarian cancer. In addition, the MAH also took this opportunity to amend section 4.4 and 4.6 to update information on contraception based on EMA and Clinical Trials Facilitation and Coordination Group (CTFG) recommendations. The package leaflet and the RMP (version 6.0) are updated accordingly

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

5.3.26. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0107

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include in combination with fluoropyrimidine- and platinum-based combination chemotherapy the first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) based on study CA209648: a randomized phase 3 study of nivolumab plus ipilimumab or nivolumab combined with fluorouracil plus cisplatin versus fluorouracil plus cisplatin in subjects with unresectable advanced, recurrent or metastatic previously untreated oesophageal squamous cell carcinoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 25.0) are updated in accordance

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

5.3.27. 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 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

5.3.28. Padeliporfin - TOOKAD (CAP) - EMEA/H/C/004182/II/0015

Applicant: STEBA Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Submission of the clinical study report for study CLIN1001 PCM301FU5 (listed as a post-authorisation efficacy study (PAES), category 1 study in Annex II): a European randomised phase 3 study to assess the efficacy and safety of Tookad (padeliporfin) soluble for localised prostate cancer compared to active surveillance. Annex II is updated to remove reference to this study. The RMP (version 8.0) is updated accordingly

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

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

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

5.3.30. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/II/0029, Orphan

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final results of study SHP634-101: an open-label, randomised, crossover study to assess the pharmacokinetic and pharmacodynamic profiles of once-daily and twice-daily dose regimens of recombinant human parathyroid hormone (rhPTH[1-84]) administered subcutaneously to subjects with hypoparathyroidism. Further clinical evaluation of an alternative dosing regimen is no longer warranted, as outlined in the current specific obligation (study SHP634-403). The conditional marketing authorisation can therefore be converted into a standard marketing authorisation (no longer subject to a specific obligation) valid for 5 years. The RMP (version 3.2) is updated accordingly

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

5.3.31. Polatuzumab vedotin - POLIVY (CAP) - EMEA/H/C/004870/II/0012, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include treatment of adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL) in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone based on the efficacy and safety data from pivotal study GO39942 (POLARIX): a phase 3, multicentre, randomized, double-blind, placebo-controlled trial comparing the efficacy and safety of polatuzumab vedotin in combination with rituximab and cyclophosphamide, doxorubicin and prednisone (CHP) (R-CHP) versus rituximab and cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) (R-CHOP) in previously untreated patients with diffuse large B-cell lymphoma. This submission fulfils SOB003 supporting the switch from conditional marketing authorisation to full marketing authorisation. As a consequence, the SmPC, Annex II and the package leaflet are revised. The RMP (version 2.0) is updated in accordance

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

5.3.32. 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

5.3.33. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0204

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nathalie Gault

Scope: Submission of the final study report for study GS-US-174-0144 (listed as category 3 study in the RMP): a randomised, double-blind evaluation of the antiviral efficacy, safety and tolerability of tenofovir disporoxil fumarate. This application fulfils the Article 46 commitment to provide the final week 192 study results for clinical measure 'study 5' (study GS_US_174-0144) listed in the paediatric investigation plan (PIP). As a consequence, section 5.1 of the SmPC is updated accordingly. Additionally, the risk minimisation measures for paediatrics are removed from the RMP and Annex II of the product information. The package leaflet and the RMP (version 25.1) are updated accordingly. In addition, the MAH took the opportunity to implement minor linguistic amendments throughout the product information. Furthermore, the expression of lactose content in Annex I for the tablets was changed to refer to lactose base (not as monohydrate) in line with current practice

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

5.3.34. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/X/0023

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new strength (200 mg solution for injection). The RMP (version 1.0) is updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Aclidinium bromide - BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP) - PSUSA/00009005/202107

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alectinib - ALECENSA (CAP) - PSUSA/00010581/202107

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alirocumab - PRALUENT (CAP) - PSUSA/00010423/202107

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/202107

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Atazanavir - REYATAZ (CAP) - PSUSA/00000258/202106

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Autologous peripheral blood T cells CD[11]4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - TECARTUS (CAP) - PSUSA/00010903/202107

Applicant: Kite Pharma EU B.V., ATMP[12]

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

[11] Cluster of differentiation
[12] Advanced therapy medicinal product

6.1.7. Avapritinib - AYVAKYT (CAP) - PSUSA/00010878/202107

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Beclometasone, formoterol, glycopyrronium bromide - RIARIFY (CAP); TRIMBOW (CAP); TRYDONIS (CAP) - PSUSA/00010617/202107

Applicant(s): Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Birch bark extract[13] - EPISALVAN (CAP) - PSUSA/00010446/202107

Applicant: Amryt GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Brexpiprazole - RXULTI (CAP) - PSUSA/00010698/202107

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Marek Juracka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Brodalumab - KYNTHEUM (CAP) - PSUSA/00010616/202107

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Budesonide[14] - JORVEZA (CAP) - PSUSA/00010664/202107

Applicant: Dr. Falk Pharma GmbH

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

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Canakinumab - ILARIS (CAP) - PSUSA/00000526/202106

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/202107

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Cenegermin - OXERVATE (CAP) - PSUSA/00010624/202107

Applicant: Dompe farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Cladribine[15] - MAVENCLAD (CAP) - PSUSA/00010634/202107

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Gefitinib - IRESSA (CAP) - PSUSA/00001518/202107

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] For treatment of multiple sclerosis only

6.1.18. Glecaprevir, pibrentasvir - MAVIRET (CAP) - PSUSA/00010620/202107

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Glucagon[16] - BAQSIMI (CAP); OGLUO (CAP) - PSUSA/00010826/202107

Applicant(s): Eli Lilly Nederland B.V. (Baqsimi), Tetris Pharma B.V. (Ogluo)

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Guselkumab - TREMFYA (CAP) - PSUSA/00010652/202107

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Human plasma protease C1 inhibitor - CINRYZE (CAP) - PSUSA/00010104/202106

Applicant: Shire Services BVBA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Ibandronic acid - BONDRONAT (CAP); BONVIVA (CAP) - PSUSA/00001702/202106

Applicant(s): Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Icosapent ethyl - VAZKEPA (CAP) - PSUSA/00010922/202107

Applicant: Amarin Pharmaceuticals Ireland Limited

PRAC Rapporteur: Menno van der Elst

[16] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Idursulfase - ELAPRASE (CAP) - PSUSA/00001722/202107

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Imipenem, cilastatin, relebactam - RECARBRIO (CAP) - PSUSA/00010830/202107

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Indacaterol, glycopyrronium, mometasone - ENERZAIR BREEZHALER (CAP); ZIMBUS BREEZHALER (CAP) - PSUSA/00010861/202107

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Inotersen - TEGSEDI (CAP) - PSUSA/00010697/202107

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. L-lysine hydrochloride, L-arginine hydrochloride - LYSAKARE (CAP) - PSUSA/00010786/202107

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Lonoctocog alfa - AFSTYLA (CAP) - PSUSA/00010559/202107

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Macimorelin - GHRYVELIN (CAP) - PSUSA/00010746/202107

Applicant: Consilient Health Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Mirabegron - BETMIGA (CAP) - PSUSA/00010031/202106

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Neratinib - NERLYNX (CAP) - PSUSA/00010712/202107

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Nivolumab - OPDIVO (CAP) - PSUSA/00010379/202107

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Osilodrostat - ISTURISA (CAP) - PSUSA/00010820/202107

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Paliperidone - INVEGA (CAP); paliperidone palmitate - BYANNLI (CAP); TREVICTA (CAP); XEPLION (CAP) - PSUSA/00002266/202106

Applicant(s): Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Peginterferon beta-1a - PLEGRIDY (CAP) - PSUSA/00010275/202107

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Perampanel - FYCOMPA (CAP) - PSUSA/00009255/202107

Applicant: Eisai GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Remimazolam - BYFAVO (CAP) - PSUSA/00010924/202107

Applicant: PAION Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Romosozumab - EVENITY (CAP) - PSUSA/00010824/202107

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Salmeterol, fluticasone propionate[17] - BROPAIR SPIROMAX (CAP); SEFFALAIR SPIROMAX (CAP) - PSUSA/00010928/202107

Applicant(s): Teva B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Saxagliptin, dapagliflozin - QTERN (CAP) - PSUSA/00010520/202107

Applicant: AstraZeneca AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - PSUSA/00010619/202107

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - PSUSA/00010630/202107

Applicant: CO.DON AG, ATMP[18]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.44. Tagraxofusp - ELZONRIS (CAP) - PSUSA/00010896/202107

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[17] Centrally authorised product(s) only
[18] Advanced therapy medicinal product

6.1.45. Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/202107

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Tobramycin[19] - TOBI PODHALER (CAP) - PSUSA/00009315/202106

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Voretigene neparvovec - LUXTURNA (CAP) - PSUSA/00010742/202107

Applicant: Novartis Europharm Limited, ATMP[20]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

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

6.2.1. 5-aminolevulinic acid[21] - AMELUZ (CAP); NAP - PSUSA/00010006/202106

Applicants: Biofrontera Bioscience GmbH (Ameluz), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Amlodipine, valsartan - COPALIA (CAP), DAFIRO (CAP), EXFORGE (CAP), NAP; amlodipine, hydrochlorothiazide, valsartan - COPALIA HCT (CAP), DAFIRO HCT (CAP), EXFORGE HCT (CAP) - PSUSA/00010344/202106

Applicants: Novartis Europharm Limited (Copalia, Copalia HCT, Dafiro, Dafiro HCT, Exforge, Exforge HCT), various

PRAC Rapporteur: Anette Kirstine Stark

[19] Inhalation powder, capsules only
[20] Advanced therapy medicinal product
[21] For treatment of keratosis only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Cabazitaxel - CABAZITAXEL ACCORD (CAP); JEVTANA (CAP); NAP - PSUSA/00000476/202106

Applicants: Accord Healthcare S.L.U. (Cabazitaxel Accord), Sanofi-aventis groupe (Jevtana), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Acenocoumarol (NAP) - PSUSA/00000027/202107

Applicant(s): various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Betula verrucosa[22] [23] (NAP) - PSUSA/00010815/202107

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Bovine lung phospholipid (NAP) - PSUSA/00010791/202106

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Calcifediol (NAP) - PSUSA/00000491/202106

Applicant(s): various

[22] Allergen for therapy
[23] Sublingual tablet(s) only

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Calcitonin salmon (NAP); synthetic analogue of eel calcitonin (NAP) - PSUSA/00000494/202106

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Cefepime (NAP) - PSUSA/00000593/202106

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Desogestrel (NAP) - PSUSA/00000966/202107

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Dexchlorpheniramine (NAP) - PSUSA/00000989/202106

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Fosinopril (NAP); fosinopril, hydrochlorothiazide (NAP) - PSUSA/00010463/202107

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Glibenclamide, metformin hydrochloride (NAP) - PSUSA/00002002/202106

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Human fibrinogen (NAP) - PSUSA/00001624/202106

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Ibuprofen, pseudoephedrine (NAP) - PSUSA/00001711/202107

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide (NAP) - PSUSA/00010390/202107

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Manidipine (NAP) - PSUSA/00001932/202106

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Nimesulide[24] (NAP) - PSUSA/00009236/202106

Applicant(s): various

PRAC Lead: Ilaria Baldelli

[24] Systemic formulation(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Propranolol[25] (NAP) - PSUSA/00010251/202106

Applicant(s): various

PRAC Lead: Guðrún Stefánsdóttir

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Rabbit anti-human T-lymphocyte immunoglobulin (NAP) - PSUSA/00010252/202106

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Solifenacin, tamsulosin (NAP) - PSUSA/00010285/202107

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Tamsulosin (NAP) - PSUSA/00002847/202107

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Thiocolchicoside (NAP); paracetamol, thiocolchicoside (NAP) - PSUSA/00010464/202107

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[25] All except centrally authorised product(s) only

6.3.21. Tiagabine (NAP) - PSUSA/00002942/202106

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Tianeptine (NAP) - PSUSA/00002943/202106

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Urapidil (NAP) - PSUSA/00003078/202107

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/LEG 015

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.2. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/LEG 010

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure

(PSUSA/00010075/202101) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.3. Dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/LEG 005

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: David Olsen

Scope: Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.4. Sitagliptin - JANUVIA (CAP) - EMEA/H/C/000722/LEG 041.1

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 041.1 [cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.5. Sitagliptin - RISTABEN (CAP) - EMEA/H/C/001234/LEG 019.1

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 019 [cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.6. Sitagliptin - TESAVEL (CAP) - EMEA/H/C/000910/LEG 035.1

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 035 [cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment

(PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.7. Sitagliptin - XELEVIA (CAP) - EMEA/H/C/000762/LEG 040.1

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 040 [cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.8. Sitagliptin, metformin hydrochloride - EFFICIB (CAP) - EMEA/H/C/000896/LEG 020.1

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 020 [cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.9. Sitagliptin, metformin hydrochloride - JANUMET (CAP) - EMEA/H/C/000861/LEG 020.1

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 020 [cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.10. Sitagliptin, metformin hydrochloride - RISTFOR (CAP) - EMEA/H/C/001235/LEG 016.1

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 016 [cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.11. Sitagliptin, metformin hydrochloride - VELMETIA (CAP) - EMEA/H/C/000862/LEG 020.1

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 020 [cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/WS2192/0075; dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/WS2192/0099; dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/WS2192/0026; dolutegravir, rilpivirine - JULUCA (CAP) - EMEA/H/C/004427/WS2192/0040

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to add completed suicide to the list of adverse drug reactions (ADRs) with a frequency rare to Tivicay (dolutegravir), Dovato (dolutegravir/lamivudine) and Triumeq (dolutegravir/ abacavir/lamivudine) following the finalisation of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) in September 2021. As the changes impact all doletugravir-containing products, Juluca (dolutegravir/rilpivirine) is also updated in accordance. The package leaflets are updated accordingly

Action: For adoption of PRAC Assessment Report

6.5.2. Macitentan - OPSUMIT (CAP) - EMEA/H/C/002697/II/0042, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of Annex II of the product information and of the RMP (version 12.1) in line with the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA/00010115/202010) adopted in June 2021 to remove the controlled distribution system and prescriber kit (prescribing check list and healthcare professional (HCP)

brochure) as additional risk minimisation measures (aRMM) while the patient alert card is kept as an aRMM. In addition, the RMP is updated to remove off-label use from the list of safety concerns, elderly patients aged over 75 years, patients with moderate to severe hepatic impairment and patients with severe renal impairment and/or undergoing dialysis as missing information. The MAH took the opportunity to include in the RMP updated specific follow-up questionnaires forms (in line with internal company template. Finally, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.2)

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[26]

6.6.1. Coronavirus (COVID-19) mRNA[27] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 011.10

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Eleventh expedited summary safety report (SSR) for Spikevax (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.2. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.11

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Twelfth expedited summary safety report (SSR) for Comirnaty (COVID-19 mRNA vaccine (nucleoside-modified)) 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)[28]

7.1.1. Afamelanotide – SCENESSE (CAP) - EMEA/H/C/PSA/S/0076.1

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSA/S/0076 [substantial amendment to a protocol previously

[26] 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
[27] Messenger ribonucleic acid
[28] In accordance with Article 107n of Directive 2001/83/EC

agreed in March 2016 (PSP/0022.1.A.1 (PSA/0002)) for study CUV-PA001: a post-authorisation disease registry safety study to generate data on the long-term safety and clinical effectiveness of Scenesse (afamelanotide) in patients with erythropoietic protoporphyria (EPP)] as per the request for supplementary information (RSI) adopted in October 2021

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

7.1.2. Chlormadinone acetate, ethinylestradiol (NAP) – EMEA/H/N/PSA/J/0072.1

Applicant: Gedeon Richter PLC

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSA/J/0072 [substantial amendment to a joint protocol previously agreed in October 2018 for a case control study comparing levonorgestrel and chlormadinone acetate to compare the risk of venous thromboembolism (VTE) of combined hormonal contraceptives (COCs) containing chlormadinone (CMA) 2mg / ethinylestradiol (EE) 30 µg, compared to COCs containing levonorgestrel (LNG) 0.15mg, both combined with 30 µg ethinylestradiol (EE)] as per the request for supplementary information (RSI) adopted in July 2021

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

7.1.3. Levonorgestrel (NAP) - EMEA/H/N/PSA/S/0073.1

Applicant: Bayer Pharma AG (Jaydess, Luadei)

PRAC Rapporteur: Annika Folin

Scope: MAH's response to PSA/S/0073 [substantial amendment to a protocol previously agreed in November 2019 (PSA/S/0044) for study EURAS-LCS12: a European active surveillance study of LCS-12 (levonorgestrel intrauterine contraceptive system releasing 12 µg levonorgestrel/24h in vitro), an intra-uterine device (IUD) for Jaydess and Luadei (levonorgestrel) to investigate whether LCS-12 is associated with an increased risk of unintended pregnancy compared to Mirena (levonorgestrel-releasing intrauterine system) and to copper IUDs] as per the request for supplementary information (RSI) adopted in September 2021

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

7.1.4. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/PSA/S/0082

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Substantial amendment to a protocol previously agreed in July 2019 (PSA/S/0040) for study TED-R13-002: a prospective, multicentre registry for patients with short bowel syndrome

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

7.1.5. Tolvaptan - JINARC (CAP) - EMEA/H/C/PSA/S/0078.1

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to PSA/S/0078 [substantial amendment to a protocol previously agreed in March 2016 (PSP/0028.2) for a 7.5-year, multicentre, non-interventional PASS to characterise and quantify the identified risk of idiosyncratic liver injury in Jinarc (tolvaptan) treated patients with autosomal dominant polycystic kidney disease (ADPKD) in routine clinical practice] as per the request for supplementary information (RSI) adopted in November 2021

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[29]

7.2.1. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 011.1

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 011 [protocol for study GS-EU-417-9050: a non-interventional post-authorisation cross-sectional safety study evaluating the effectiveness of the additional risk minimisation measures for filgotinib use in patients with rheumatoid arthritis within the German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

7.2.2. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/MEA 015.4

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Amendment to a protocol previously agreed in September 2018 for study NN8022-4246: a drug utilisation study (DUS) in the United Kingdom using UK clinical practice research datalink (CPRD) database evaluating if liraglutide (Saxenda) is used according to approved indication and posology and if liraglutide (Victoza) is used for weight management

Action: For adoption of advice to CHMP

7.2.3. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.11

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

[29] 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

Scope: MAH's response to MEA 003.10 [third feasibility assessment report and protocol for study NB-451: an observational retrospective drug utilisation study (DUS) of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) in Europe and the United States to describe the demographic and baseline characteristics of users of Mysimba (naltrexone hydrochloride/bupropion hydrochloride), evaluate patterns of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) initiation and use] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

7.2.4. Risdiplam - EVRYSDI (CAP) - EMEA/H/C/005145/MEA 007.1

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: MAH's response to MEA 007 [protocol for study BN42833 - Risdiplam pregnancy surveillance study: a phase 4, non-interventional surveillance study [final study report expected in Q4/2031] (from initial opinion/marketing authorisation (MA)] as per request for supplementary information (RSI) adopted in October 2021

Action: For adoption of advice to CHMP

7.2.5. Setmelanotide - IMCIVREE (CAP) - EMEA/H/C/005089/MEA 001

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Marek Juracka

Scope: Protocol for study RM-IMC-901 (listed as a category 3 study in the RMP): a registry of patients with biallelic homozygous pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency obesity treated with setmelanotide (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.2.6. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.2

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 010.1 [amendment to a protocol previously agreed in the initial marketing authorisation application (MAA)/marketing authorisation for study C4591012 assessing the occurrence of safety events of interest, including severe or atypical COVID-19 in real-world use of COVID-19 mRNA vaccine to include the booster dose [final clinical study report (CSR) expected in December-2023]] as per the request for supplementary information (RSI) adopted in November 2021

Action: For adoption of advice to CHMP

7.2.7. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 041

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study C4591036 (former paediatric heart network study): a safety surveillance study of myocarditis and myopericarditis associated with Comirnaty (tozinameran) in persons less than 21 years of age to characterize the clinical course, risk factors, long-term sequelae, and quality of life in children and young adults under 21 years with acute post-vaccine myocarditis

Action: For adoption of advice to CHMP

7.2.8. Upadacitinib – RINVOQ (CAP) – EMEA/H/C/004760/MEA 012

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study P21-825: an evaluation of the effectiveness of additional risk minimisation measures for upadacitinib in the treatment of atopic dermatitis

Action: For adoption of advice to CHMP

7.2.9. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 013

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study P20-390: a cohort study of long-term safety of upadacitinib in the treatment of atopic dermatitis in Denmark and Sweden

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[30]

7.3.1. Aprotinin (NAP) - EMEA/H/N/PSR/S/0030

Applicant: Nordic Group BV (Trasylol)

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to PSR/S/0030 [results for a Nordic aprotinin patient registry to record utilisation information on patients at cardiac surgery centres] as per the request for supplementary information (RSI) adopted in September 2021

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

7.3.2. Human normal immunoglobulin - HYQVIA (CAP) - EMEA/H/C/PSR/S/0037

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Results of study number 161302 (listed as a category 1 study in Annex II and the

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

RMP): non-interventional post-authorization safety study on the long-term safety of Hyqvia in subjects treated with Hyqvia (human normal immunoglobulin)

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

7.3.3. Hydroxyethyl starch (HES) (NAP) - EMEA/H/N/PSR/J/0031

Applicant(s): B. Braun Melsungen AG (Tetraspan, Venofundin), Fresenius Kabi Deutschland GmbH (Volulyte, Voluven)

PRAC Rapporteur: Nathalie Gault

Scope: MAH's response to PSR/J/0031 [results for a joint retrospective, multinational, drug utilisation study (DUS) to assess the non-adherence of physicians in hydroxyethyl starch (HES) accredited hospitals to the approved European product information [regarding indication for use, contraindications and posology (dosage)] for HES 130-containing medicinal products in clinical routine after implementation of a set of risk minimisation measures as required in the outcome of the referral procedure under Article 107i of Directive 2001/83/EC for HES completed in 2018 (EMEA/H/A-107i/1457)] as per the request for supplementary information (RSI) adopted in January 2022

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)[31]

7.4.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0040, Orphan

Applicant: Kite Pharma EU B.V., ATMP[32]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final study report for non-interventional study KT-EU-471-0116 (listed as category 3 study in the RMP): a quantitative testing of healthcare provider knowledge about Yescarta (axicabtagene ciloleucel) risk minimisation measures

Action: For adoption of PRAC Assessment Report

7.4.2. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0038

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study MS1222-0003 (listed as a category 3 study in the RMP) as assessment of anti-platelet factor 4 (PF4) antibodies prior to, and following, vaccination with AZD1222: a study where sera of vaccinated individuals in study D8110C00001 are tested to elucidate whether vaccination with Vaxzevria (COVID-19

[31] 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
[32] Advanced therapy medicinal product

vaccine) leads to increased levels of circulating anti-PF4 antibodies, a key component of the hypothesised mechanism underlying thrombosis with thrombocytopenia syndrome (TTS)

Action: For adoption of PRAC Assessment Report

7.4.3. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/WS2078/0034; ROTEAS (CAP) - EMEA/H/C/004339/WS2078/0020

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Nathalie Gault

Scope: Submission of the final report from study ETNA-VTE-EUROPE (DSE-EDO-05-14-EU), (listed as a category 3 study in the RMP): a non-interventional study on edoxaban treatment in routine clinical practice in patients with venous thromboembolism in Europe. The RMP (version 12.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/WS2196/0063; empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/WS2196/0042; empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/WS2196/0060

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Update of section 4.4 of the SmPC to delete the warning on lower limb amputations based on the results from the final meta-analysis report of study 1245.171 (listed as category 3 study in the RMP): a meta-analysis of amputation risk in empagliflozin studies, namely: 1) study 1245.25 (EMPA-REG OUTCOME): a study in patients with type 2 diabetes mellitus (T2DM) and increased cardiovascular risk; 2) study 1245.110 (EMPEROR- HFpEF): a study in patients with chronic heart failure (HF) with preserved ejection fraction; 3) study 1245.121 (EMPEROR- HFrEF): a study in patients with chronic HF with reduced ejection fraction. The package leaflet and the RMP (version 17 for Jardiance, version 11 for Synjardy and version 6 for Glyxambi) are updated accordingly. The conduct of this meta-analysis was requested to MAHs of all sodium-glucose co-transporter-2 (SGLT2)-containing products as part of the outcome of the referral procedure (EMEA/H/A-20/1419) under Article 20 of Regulation (EC) No 726/2004 finalised in 2016

Action: For adoption of PRAC Assessment Report

7.4.5. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/II/0244

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final report from study B1801310 (BIKER) (listed as a category 3 study in the RMP): an observational PASS of etanercept and methotrexate in the treatment of juvenile idiopathic arthritis (JIA) using data obtained from participants in the German Biologics JIA registry (BIKER) to monitor long-term safety and effectiveness of etanercept in the treatment of JIA in regular clinical practice

Action: For adoption of PRAC Assessment Report

7.4.6. 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 post-authorisation safety study (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

7.4.7. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0054

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study NB-542 (listed as a category 3 study in the RMP): a cross-sectional survey aimed to evaluate the effectiveness of the Mysimba (naltrexone hydrochloride/bupropion hydrochloride) physician prescribing checklist (PPC) among physicians in the EU. The RMP (version 12.6) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/II/0083

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final report from study 20070797 (listed as a category 3 study in the RMP): an observational study assessing the long-term safety of romiplostim treatment in real-life clinical practice in three Nordic countries. The RMP (version 21.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.9. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0091

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final safety registry report from study CNTO1275PSO4007: pregnancy research initiative - exposure to ustekinumab during pregnancy: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers (in fulfilment of MEA 024). The RMP (version 22.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 075.10

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of advice to CHMP

7.5.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 080.8

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of advice to CHMP

7.5.3. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 009.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Third interim report for study MB102-118 ST/D1690R00007 - (EUPAS12116): a pharmacoepidemiology study assessing the risk of cancer [final clinical study report (CSR) expected in 2024]

Action: For adoption of advice to CHMP

7.5.4. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/MEA 004.8

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Third interim report for study MB102-118 ST/D1690R00007 (EUPAS12116): a pharmacoepidemiology study assessing the risk of cancer [final clinical study report (CSR)

due in 2024]

Action: For adoption of advice to CHMP

7.5.5. Filgrastim - NIVESTIM (CAP) - EMEA/H/C/001142/MEA 015.6

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Fifth annual report for study ZOB-NIV-1513 (C1121008): a multinational, multicentre, prospective, non-interventional PASS in healthy donors (HDs) exposed to Nivestim (biosimilar filgrastim) for haematopoietic stem cell (HSC) mobilisation (NEST) [final clinical study report (CSR) expected in March 2023]

Action: For adoption of advice to CHMP

7.5.6. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/ANX 001.4

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Fourth annual interim study report for study P15-11: a 5-year multicentre, observational PASS to document the utilisation of Wakix (pitolisant) in the treatment of narcolepsy with or without cataplexy and to collect information on its long-term safety when used in routine medical practice [final results expected in 2023]

Action: For adoption of advice to CHMP

7.5.7. Sebelipase alfa - KANUMA (CAP) - EMEA/H/C/004004/ANX 001.5

Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of advice to CHMP

7.5.8. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005.3

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Annual progress reports 2021 for: 1) pregnancy registry OBS12751 (international): an international pregnancy exposure registry of women with multiple sclerosis (MS) exposed to Aubagio (teriflunomide) and; 2) pregnancy registry OBS13499 (US/CA): teriflunomide pregnancy outcome exposure registry: a 'teratology information specialists (OTIS)' autoimmune diseases in pregnancy project

Action: For adoption of advice to CHMP

7.5.9. Turoctocog alfa pegol - ESPEROCT (CAP) - EMEA/H/C/004883/ANX 001.1

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: First annual progress report for study NN7088-4029: a multinational, prospective, open labelled, non-controlled, non-interventional PASS of turoctocog alfa pegol (N8-GP) during long-term routine prophylaxis and treatment of bleeding episodes in patients with haemophilia A

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/MEA 002.2

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: MAH's response to MEA 002.1 [protocol for study D8220C00008 (listed as a category 3 study in the RMP): a phase 3b, multicentre, open-label, single-arm study in subjects with chronic lymphocytic leukaemia (ASSURE) to address missing information around moderate to severe cardiac impaired patients in subjects treated with Calquence (acalabrutinib)] as per the request for supplementary information (RSI) adopted in October 2021

Action: For adoption of advice to CHMP

7.6.2. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 007.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Statistical analysis plan (SAP) for study D8111R00006: a post-authorisation/post-marketing observational study using existing secondary health data sources to evaluate the association between exposure to Vaxzevria (AZD1222) and safety concerns

Action: For adoption of advice to CHMP

7.6.3. Eribulin - HALAVEN (CAP) - EMEA/H/C/002084/MEA 024.2

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: MAH's justification to request an extension of the due date of the final study report for study E7389-M044-504 (IRENE): an observational, post-authorisation, single-arm, prospective, multicentre cohort study to characterise and determine the incidence of eribulin-induced peripheral neuropathy (PN), and the frequency and time to resolution of eribulin-induced PN in adult patients treated with eribulin in a real-life setting with locally advanced or metastatic breast cancer who have progressed after at least one

chemotherapeutic regimen for advanced disease

Action: For adoption of advice to CHMP

7.6.4. Insulin detemir - LEVEMIR (CAP) - EMEA/H/C/000528/MEA 045.11

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of a statement to clinical overview addendum in order to correct some discrepancies related to post-marketing data from non-interventional study NN304-4016 (listed as a category 3 study in the RMP): a diabetes pregnancy registry study conducted to assess the long-term safety of insulin use in pregnant women (in fulfilment of MEA 045)

Action: For adoption of PRAC Assessment Report

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. 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

8.1.2. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0048 (without RMP)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Obiltoxaximab - OBILTOXAXIMAB SFL (CAP) - EMEA/H/C/005169/S/0004 (without RMP)

Applicant: SFL Pharmaceuticals Deutschland GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. 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

8.1.5. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/S/0076 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.6. Tocofersolan - VEDROP (CAP) - EMEA/H/C/000920/S/0041 (without RMP)

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

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. Onasemnogene abeparvovec - ZOLGENSMA (CAP) - EMEA/H/C/004750/R/0021 (without RMP)

Applicant: Novartis Gene Therapies EU Limited, ATMP[33]

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

[33] Advanced therapy medicinal product

Action: For adoption of advice to CAT and CHMP

8.2.2. Selumetinib - KOSELUGO (CAP) - EMEA/H/C/005244/R/0003 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Adalimumab - IMRALDI (CAP) - EMEA/H/C/004279/R/0050 (without RMP)

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/R/0069 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/R/0019 (with RMP)

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/R/0022 (with RMP)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Fampridine - FAMPYRA (CAP) - EMEA/H/C/002097/R/0050 (without RMP)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/R/0106 (without RMP)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Meningococcal group b vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/R/0036 (with RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Midostaurin - RYDAPT (CAP) - EMEA/H/C/004095/R/0023 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Rituximab - BLITZIMA (CAP) - EMEA/H/C/004723/R/0049 (without RMP)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/R/0029 (with RMP)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/R/0053 (with RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - EMEA/H/C/002736/R/0024 (with RMP)

Applicant: CO.DON AG, ATMP[34]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.3.13. 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

[34] Advanced therapy medicinal product

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Infliximab – REMICADE (CAP) - EMEA/H/C/000240/IB/0233

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: PRAC consultation on a variation updating sections 4.4, 4.5 and 4.6 of the SmPC, the patient reminder card in Annex II with regards to the administration of live vaccines to infants following in utero exposure to Remicade (infliximab) as per the outcome of post-authorisation measure (LEG 159.2) adopted in November 2021. The package leaflet is updated accordingly

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

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. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q4 2021

Action: For discussion

12.1.3. Vote by proxy

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Classification of post-authorisation studies group (CPAS) - activities overview

Action: For discussion

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. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q4 2021 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q4 2021

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

12.14.3. Coronavirus (COVID-19) pandemic - coreRMP19: update

PRAC lead: Jean-Michel Dogné, Brigitte Keller-Stanislawski, Zane Neikena, Hans Christian Siersted, Anette Kirstine Stark, Menno van der Elst, Ulla Wändel Liminga

Action: For adoption

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. EU pharmaceutical legislation – revision of Directive 2001/83/EC and Regulation (EC) No 726/2004

PRAC lead: Amelia Cupelli, Maria del Pilar Rayon, Liana Gross-Martirosyan, Martin Huber, Eva Segovia, Sabine Straus, Menno van der Elst, Ulla Wändel Liminga

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, 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