05 June 2023
EMA/PRAC/215930/2023 Corr[1]
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 05-08 June 2023

Chair: Sabine Straus – Vice-Chair: Martin Huber

05 June 2023, 13:00 – 19:45, room 2C / via teleconference

06 June 2023, 09:00 – 19:45, room 2C / via teleconference

07 June 2023, 09:00 – 19:45, room 2C / via teleconference

08 June 2023, 09:00 – 16:00, room 2C / via teleconference

Organisational, regulatory and methodological matters (ORGAM)

22 June 2023, Time, 09:00 - 12:00, via teleconference

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

[1] 06 June 2023 - Crizanlizumab - ADAKVEO (CAP) - PSUSA/00010888/202211 – update of action

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

Table of contents

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 05-08 June 2023. See June 2023 PRAC minutes (to be published post July 2023 PRAC meeting).

1.2. Agenda of the meeting on 05-08 June 2023

Action: For adoption

1.3. Minutes of the previous meeting on 09-12 May 2023

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. Topiramate (NAP); topiramate, phentermine (NAP) - EMEA/H/A-31/1520

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Martin Huber

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

Action: For adoption of a 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

4.1.1. Amivantamab - RYBREVANT (CAP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of anaphylactic reaction

Action: For adoption of PRAC recommendation

EPITT 19928 – New signal

Lead Member State(s): DE

[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

4.1.2. Dapagliflozin – EDISTRIDE (CAP), FORXIGA (CAP), EBYMECT (CAP), XIGDUO (CAP), QTERN (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: to be appointed

Scope: Signal of acquired phimosis and phimosis with dapagliflozin

Action: For adoption of PRAC recommendation

EPITT 19935 – New signal

Lead Member State(s): SE

4.1.3. Leuprorelin – CAMCEVI (CAP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of severe cutaneous adverse reactions (SCARS)

Action: For adoption of PRAC recommendation

EPITT 19930 – New signal

Lead Member State(s): IT

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Ipilimumab – YERVOY (CAP) - EMEA/H/C/002213/SDA/046; nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/SDA/051; pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/036

Applicant(s): Bristol-Myers Squibb Pharma EEIG (OPDIVO, YERVOY), Merck Sharp & Dohme B.V. (KEYTRUDA)

PRAC Rapporteur: Menno van der Elst

Scope: Signal of capillary leak syndrome (OPDIVO, YERVOY, KEYTRUDA) and cytokine release syndrome (OPDIVO)

Action: For adoption of PRAC recommendation

EPITT 19880 – follow up to February 2023

4.3.2. Tofacitinib – XELJANZ (CAP) - EMEA/H/C/004214/SDA/026

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of acnes

Action: For adoption of PRAC recommendation

EPITT 19885 – follow up to February 2023

4.4. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Dantrolene sodium, hemiheptahydrate - EMEA/H/C/006009, Orphan

Applicant: Norgine B.V.

Scope: treatment of malignant hyperthermia (including suspected cases)

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

5.1.2. Fezolinetant - EMEA/H/C/005851

Scope: treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause

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

5.1.3. Latanoprost - EMEA/H/C/005933

Scope: reduction of elevated intraocular pressure (IOP)

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

5.1.4. Methylphenidate hydrochloride - EMEA/H/C/005975, PUMA[4]

Scope: treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children aged 6 years of age and over

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

5.1.5. Zilucoplan - EMEA/H/C/005450, Orphan

Applicant: UCB Pharma S.A.

Scope: treatment of generalised myasthenia gravis in adults

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

[4] Paediatric-use marketing authorisation(s)

5.2. Medicines in the post-authorisation phase – PRAC-led procedures

5.2.1. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0085

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of an updated RMP version 21.0 in order to include the physician survey CICL670A2429 as a PASS category 3, based on the submission of a draft version of the protocol for the physician survey CICL670A2429. The Annex IID is updated to remove one sentence related to 'surveillance programme' and to introduce a minor correction

Action: For adoption of PRAC Assessment Report

5.2.2. Dexamethasone - OZURDEX (CAP) - EMEA/H/C/001140/II/0044

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of an updated Annex II and RMP version 11 in order to remove additional risk minimisation measure: Patient guide, audio CD (where required)

Action: For adoption of PRAC Assessment Report

5.2.3. Esomeprazole - NEXIUM CONTROL (CAP) - EMEA/H/C/002618/II/0038

Applicant: GlaxoSmithKline Dungarvan Ltd

PRAC Rapporteur: Rugile Pilviniene

Scope: Submission of an updated RMP version 2.0 in order to update the list of safety concerns to meet the definition of important risk and missing information provided in GVP Module V Rev. 2

Action: For adoption of PRAC Assessment Report

5.2.4. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0017, Orphan

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 2.10 in order to implement a targeted follow-up questionnaire (FUQ) to further improve the collection of follow-up information on cases of vascular heart disease (VHD) and pulmonary arterial hypertension (PAH) suggested by PRAC following PSUSA/00010907/2021122

Action: For adoption of PRAC Assessment Report

5.2.5. Glycopyrronium - SIALANAR (CAP) - EMEA/H/C/003883/II/0026

Applicant: Proveca Pharma Limited

PRAC Rapporteur: Zane Neikena

Scope: Submission of an updated RMP version 3.1 in order to remove a Drug Utilisation Study (DUS). Furthermore, Annex II D "Conditions or restrictions with regard to the safe and effective use of the medicinal product" was revised to delete from the key elements of the physician educational material information about the utilisation study

Action: For adoption of PRAC Assessment Report

5.2.6. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/WS2487/0199; LIPROLOG (CAP) - EMEA/H/C/000393/WS2487/0159

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Mari Thorn

Scope: To remove severe hypoglycemia as a result of incorrect or incomplete data provided to a compatible software application which is listed as an important potential risk for the Tempo Pen and all associated risk minimisation measures, following PRAC assessment of F3Z-MC-B030 PASS protocol (following MEA 035 concluded in October[5] 2022)

Action: For adoption of PRAC Assessment Report

5.2.7. Laronidase - ALDURAZYME (CAP) - EMEA/H/C/000477/II/0085

Applicant: Sanofi B.V.

PRAC Rapporteur: Nathalie Gault

Scope: To update section 4.2 of the SmPC in order to modify the administration instructions following the periodic safety update single assessment (PSUSA) procedure (PSUSA/00001830/202104) adopted in December[6] 2021 based on literature review. The package leaflet is updated accordingly. The RMP version 1.0 has also been submitted

Action: For adoption of PRAC Assessment Report

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

5.3.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/X/0084/G

Applicant: Bayer AG

PRAC Rapporteur: Nathalie Gault

Scope: Extension application to add a new strength of Aflibercept 114.3 mg/ml solution for injection (in a vial), to be indicated in adults for the (1) treatment of neovascular (wet) age-related macular degeneration (nAMD) and (2) visual impairment due to diabetic macular oedema (DME), grouped with a type II variation (B.II.g.2) to introduce a post-approval change management protocol to add a new presentation for Aflibercept solution 114.3 mg/ml in a single-use pre-filled syringe for intravitreal injection

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

[5] Held on 26-29 September 2022
[6] Held 29 November – 02 December 2021

5.3.2. Agomelatine - VALDOXAN (CAP) - EMEA/H/C/000915/II/0051

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Pernille Harg

Scope: Extension of indication to include new therapeutic indication in adolescents aged 12 to 17 years for the treatment of moderate to severe major depressive episodes, if depression is unresponsive to psychological therapy alone, for Valdoxan, further to the results of the phase 2 (CL2-20098-075) and phase 3 (CL3-20098-076) paediatric clinical studies included in the Paediatric Investigation Plan number EMEA-001181-PIP-11; As a consequence the sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly. The updated RMP version 25.1 has also been submitted

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

5.3.3. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/II/0078

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of paediatric patients 8 years of age and older with heterozygous familial hypercholesterolemia (HeFH) as an adjunct to diet, alone or in combination with other LDL-C lowering therapies, based on final results from study EFC14643 listed as a category 3 study in the RMP; this is a randomised, double-blind, placebo-controlled study followed by an open-label treatment period to evaluate the efficacy and safety of alirocumab in children and adolescents with heterozygous familial hypercholesterolemia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 8.0 of the RMP is also submitted

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

5.3.4. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/II/0018

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.5 and 5.2 of the SmPC in order to update drug-drug interaction information, based on final results from study BYL719A2111; this is a phase 1, open-label, fixed-sequence, two-period drug-drug interaction (DDI) study evaluating the PK probe substrates for CYP3A4, CYP2B6, CYP2C8, CYP2C9, and CYP2C19 when administered either alone or in combination with repeated doses of alpelisib. The Annex II and package leaflet are updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.5. Bezlotoxumab - ZINPLAVA (CAP) - EMEA/H/C/004136/II/0037

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of the paediatric population (1 to 18 years of age) for ZINPLAVA, based on final results from study MK-6072-001 (MODIFY III) listed as a category 3 study in the RMP; this is a phase 3, randomised, placebo-controlled, parallel-group, multi-site, double-blind trial evaluating the safety, tolerability, pharmacokinetics (PK) and efficacy of a single infusion of bezlotoxumab in paediatric participants from 1 to <18 years of age receiving antibacterial drug treatment for Clostridioides difficile infection (CDI). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.3 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the product information

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

5.3.6. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0107, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of adult patients with previously untreated CD30+ advanced (including Stage III) Hodgkin lymphoma (HL), in combination with doxorubicin, vinblastine and dacarbazine (AVD), for ADCETRIS, based on the second interim analysis of overall survival (OS) data from ECHELON-1 study (C25003); this is a randomised, open-label, phase 3 trial of A+AVD versus ABVD as frontline therapy in patients with advanced classical HL. As a consequence, sections 4.1 and 5 of the SmPC are updated

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

5.3.7. Carglumic acid - CARBAGLU (CAP) - EMEA/H/C/000461/II/0045

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to include a proposed dose adjustment for patients with impaired renal function based on final results from study RCD-P0-027; this is a Phase I, multicenter, open-label, parallel-group adaptive pharmacokinetic single dose study of oral Carbaglu in subjects with normal and varying degrees of impaired renal function. The package leaflet is updated accordingly. The RMP version 2.2 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in Annex II and Labelling, and to bring the product information in line with the latest QRD template version 10.3

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

5.3.8. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - EMEA/H/C/002246/II/0058

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Extension of current indication for removal of eschar in adults with deep partial- and full-thickness thermal burns to the paediatric population for NexoBrid based on interim results from study MW2012-01-01 (CIDS study), listed as Study MW2012-01-01 is a 3-stage, multi-centre, multi-national, randomised, controlled, open label, 2-arm study aiming to demonstrate the superiority of NexoBrid treatment over standard of care (SOC) treatment in paediatric patients (aged 0 to 18 years) with deep partial thickness (DPT) and full thickness (FT) thermal burns of 1% to 30% of total body surface area (TBSA). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated accordingly. Version 9 of the RMP has also been submitted

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

5.3.9. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0126, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Monica Martinez Redondo

Scope: Extension of indication to include treatment of paediatric patients with refractory generalised myasthenia gravis (gMG) for Soliris, based on interim results from study ECU-MG-303; this is an open-label, multicentre, phase 3 study to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of intravenous (IV) eculizumab in paediatric patients aged 6 to less than 18 years with acetylcholine receptor-antibody (AChR-Ab) positive (+) refractory gMG. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 20.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to update section 4.8 of the SmPC in order to update the frequency of the list of adverse drug reactions (ADRs) based on cumulative safety data and to introduce minor editorial changes to the product information

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

5.3.10. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0104/G

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Grouped variation consisting of: 1) Extension of indication to include the use of Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection as a two-dose primary vaccination course in children 6 months through 5 years of age, based on data from study mRNA-1273-P306 (NCT05436834), an Open-Label, Phase 3 Study to Evaluate the Safety and Immunogenicity of the mRNA-1273.214 Vaccine for SARS-CoV-2 Variants of Concern in Participants Aged 6 Months to < 6 Years; as a consequence, sections 2, 4.1, 4.2 and 6.6 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. Version 6.7 of the RMP has also been submitted; 2) Extension of indication to include the use of Spikevax bivalent Original/Omicron BA.4-5 as a single-dose primary vaccination course against COVID-19 in individuals 6 years of age and older, irrespective of vaccination history, based on epidemiology and clinical data from Study P306 Part 1; as a consequence, sections 2, 4.1, 4.2 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial

changes/corrections throughout the product information

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

5.3.11. Faricimab - VABYSMO (CAP) - EMEA/H/C/005642/II/0002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information and to update the warnings and the list of adverse drug reactions (ADRs), based on longer-term results from studies GR40306 (TENAYA) and GR40844 (LUCERNE); these are phase 3, multicentre, randomised, double-masked, active comparator-controlled, 112-week studies to evaluate the efficacy and safety of faricimab in patients with neovascular age-related macular degeneration (nAMD); the package leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.12. Gilteritinib - XOSPATA (CAP) - EMEA/H/C/004752/II/0013, Orphan

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.2 and 5.2 in order to update the information on renal impairment based on final results from study 2215-CL-0114, listed as a category 3 study in the RMP. Study 2215-CL-0114 is a phase 1, single-dose, open-label study to investigate the effect of renal impairment on gilteritinib pharmacokinetics, safety and tolerability in 9 participants with severe renal impairment compared to 8 participants with normal renal function. The RMP version 4.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes

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

5.3.13. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0011/G, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped variation consisting of: 1) update of section 5.3 of the SmPC based on final results from study AS1-GLP18-007 listed as a category 3 study in the RMP: a 104-week subcutaneous injection carcinogenicity study in Sprague Dawley rats; 2) update of section 5.3 of the SmPC based on final results from study AS1-GLP18-004: a 26-week subcutaneous injection carcinogenicity study in TgRasH2 mice. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.14. Human coagulation factor X - COAGADEX (CAP) - EMEA/H/C/003855/II/0046, Orphan

Applicant: BPL Bioproducts Laboratory GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study TEN06 - NCT03161626 (REC EMEA/H/C/003855). This is a non-interventional, multicenter, post-marketing registry study in three patients with moderate or severe hereditary FX deficiency, to assess Coagadex administered peri-operatively for haemostatic cover in major surgery during routine post-marketing use. The primary objective is to collect additional surgical data on the clinical effectiveness of Coagadex, in a post-marketing environment, for peri-operative haemostatic cover during major surgery in patients with moderate or severe hereditary factor X (FX) deficiency. The RMP version 3.0 has also been submitted

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

5.3.15. Idecabtagene vicleucel - ABECMA (CAP) - EMEA/H/C/004662/II/0031, Orphan

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP[7]

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of adult patients with relapsed and refractory multiple myeloma (RRMM) who have received at least two prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD-38 antibody and have demonstrated disease progression on the last therapy for Abecma (idecabtagene vicleucel, ide-cel), based on results from study BB2121-MM-003 (MM-003, KarMMa-3). This is a Phase 3, multicentre, randomised, open-label study to compare the efficacy and safety of ide-cel versus standard regimens in subjects with RRMM. As a consequence, sections 2.1, 2.2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 6.3, 6.4 and 6.6 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. Version 3.0 of the RMP has also been submitted. Furthermore, the product information is brought in line with the Guideline on core SmPC, Labelling and package leaflet for advanced therapy medicinal products (ATMPs) containing genetically modified cells

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

5.3.16. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/II/0130

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study MA-VA-MEDI3250-1116 (A Case Control Study of the Effectiveness of quadrivalent live attenuated influenza vaccine (Q/LAIV) Versus Inactivated Influenza Vaccine and No Vaccine in Subjects 2 to 17 Years of Age) listed as a category 3 study in the RMP. This was an observational study. The objective of this study was to evaluate the effectiveness of Q/LAIV compared to IIV or no vaccine in community-

[7] Advanced therapy medicinal product

dwelling subjects 2 to 17 years of age against laboratory-confirmed influenza. The RMP version 11.0 has also been submitted

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

5.3.17. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0123

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 4.4 of the SmPC, Annex IID and Article 127a and the tools/documents included in the Educational Healthcare Professional Kit, in order to harmonise the terminology utilised in the RMP and product information documents relating to the safety concern of teratogenicity and its risk minimisation measure of the Pregnancy Prevention Plan (PPP) across the 3 immunomodulatory imide drugs (IMiDs). These proposed changes will only have a limited impact on the National Competent Authority (NCA)-approved content/text of the educational materials, and the key messages to the HCP and patients. Furthermore, the regulatory obligations regarding the PPP will not be impacted. The MAH is also taking the opportunity to update the RMP with PASS Protocol milestones. The updated RMP version 38 was provided

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

5.3.18. Letermovir - PREVYMIS (CAP) - EMEA/H/C/004536/II/0033/G, Orphan

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped application consisting of 1) Extension of indication to include treatment of prophylaxis of cytomegalovirus in kidney transplant recipients (KTR) for PREVYMIS, based on final results from study P002MK8228; this is a Phase III, randomised, double-blind, active comparator-controlled study to evaluate the efficacy and safety letermovir versus valganciclovir for the prevention of Human Cytomegalovirus (CMV) Disease in adult kidney transplant recipients. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes; 2) Update of section 4.2 of the SmPC in order to update duration of treatment recommendation based on final results from study P040MK8228; this is a Phase III randomised, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of letermovir (LET) prophylaxis when extended from 100 days to 200 days post-transplant in cytomegalovirus (CMV) seropositive recipients (R+) of an allogeneic hematopoietic stem cell transplant (HSCT)

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

5.3.19. Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/II/0021, Orphan

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Jo Robays

Scope: Extension of indication to include treatment of adult patients with anaemia due to

very low, low and intermediate-risk myelodysplastic syndromes (MDS), who may require RBC transfusions for Reblozyl, based on results from study ACE-536-MDS-002 (COMMANDS), an active-controlled, open-label, randomised Phase 3 study comparing the efficacy and safety of luspatercept vs epoetin alfa in adult subjects with anemia due to IPSS-R very low, low or intermediate risk MDS, who are ESA naïve and require RBC transfusions, and studies ACE-536-MDS-001(MEDALIST), ACE-536-MDS-004 , A536-03, A536-05 and ACE-536-LTFU-001. 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 is updated in accordance. Version 2.0 of the RMP has also been submitted

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

5.3.20. Melphalan flufenamide - PEPAXTI (CAP) - EMEA/H/C/005681/II/0002

Applicant: Oncopeptides AB

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of patients with multiple myeloma who have received at least two prior lines of therapies before PEPAXTI, based on final results from study OP-103 OCEAN; this is a randomised, open-label phase III study in patients with relapsed or refractory multiple myeloma following two to four lines of prior therapies and who were refractory to lenalidomide and the last line of therapy. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC

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

5.3.21. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/X/0052/G

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Grouped application consisting of: 1) Extension application to add a new strength of 25 mg soft capsule; 2) Addition of a new indication of treatment of fibrosing interstitial lung diseases (ILDs) in children and adolescents from 6 to 17 years of age, based on results from study 1199 0337 (InPedILD); a randomised, placebo-controlled, double-blind, multicentre, multinational, phase III clinical trial undertaken to evaluate dose-exposure and safety of nintedanib on top of standard of care in children and adolescents (6 to 17 years old) with clinically significant fibrosing ILD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes to the list of local representatives in the package leaflet. The updated RMP version 12.0 is also submitted

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

5.3.22. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/II/0032

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment and prophylaxis of bleeding in children below 12 years of age with haemophilia B including previously untreated patients for REFIXIA, based on interim results from studies NN7999-3774 and NN7999-3895. NN7999-3774 is a multicentre, open-label, non-controlled study evaluating the safety, efficacy and pharmacokinetics of nonacog beta pegol in previously treated children with haemophilia B, while NN7999-3895 is a multicentre, open-label, single-arm, non-controlled trial evaluating the safety and efficacy of nonacog beta pegol in previously untreated patients with haemophilia B. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated accordingly. Version 5.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.23. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/II/0011, Orphan

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of cholestasis and pruritus in Alagille syndrome (ALGS) in patients from birth and older for BYLVAY, based on final results from Study A4250-012 and interim results from Study A4250-015. Study A4250-012 is a 24-week, randomised, double-blind, placebo-controlled Phase III study conducted in 52 patients with a genetically confirmed diagnosis of ALGS and presence of pruritus and high serum bile acid levels at baseline. Study A4250-015 is an ongoing 72-week open-label extension trial for patients who completed Study A4250-012 and evaluates the long-term safety and efficacy of Bylvay in patients with ALGS. As a consequence, sections 4.1, 4.2, 4.8, 5.1, and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted

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

5.3.24. Omalizumab - XOLAIR (CAP) - EMEA/H/C/000606/X/0115/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Extension application to add a new strength of 300 mg (150 mg/ml) for Xolair solution for injection grouped with quality type II, IB and IAIN variations. The RMP (version 17.0) is updated in accordance.

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

5.3.25. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0134

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include pembrolizumab in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant, treatment of resectable Stage II, IIIA, or IIIB (T3 4N2) non-small cell lung

carcinoma in adults for Keytruda based on study KEYNOTE-671, a phase III, randomised, double-blind trial of platinum doublet chemotherapy +/- pembrolizumab as neoadjuvant/adjuvant therapy for participants with resectable stage II, IIIA, and resectable IIIB (T3-4N2) non-small cell lung cancer. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 41.1 of the RMP has also been submitted

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

5.3.26. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0135

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include pembrolizumab in combination with chemotherapy the first-line treatment of locally advanced unresectable or metastatic HER2-negative gastric or gastrooesophageal junction adenocarcinoma in adults based on study KEYNOTE-859, a randomised, double-blind phase 3 trial, evaluating KEYTRUDA in combination with chemotherapy compared to placebo in combination with chemotherapy for the first-line treatment of patients with HER2-negative locally advanced unresectable or metastatic gastric or esophagogastric junction (GEJ) adenocarcinoma. As a consequence sections 4.1 and 5.1 of the SmPC are updated. The package leaflet and Annex II are updated in accordance. Version 42.1 of the RMP has also been submitted

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

5.3.27. Pomalidomide - IMNOVID (CAP) - EMEA/H/C/002682/II/0047, Orphan

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Update of section 4.4 of the SmPC, Annex IID and Article 127a and the tools/documents included in the Educational Healthcare Professional Kit, in order to harmonise the terminology utilised in the RMP and product information documents relating to the safety concern of teratogenicity and its risk minimisation measure of the Pregnancy Prevention Plan across the 3 immunomodulatory imide drugs (IMiDs). These proposed changes will only have a limited impact on the National Competent Authority (NCA)-approved content/text of the educational materials, and the key messages to the HCP and patients. Furthermore, the regulatory obligations regarding the pregnancy prevention plan (PPP) will not be impacted. The updated RMP version 16 was provided

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

5.3.28. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/II/0012

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4 and 4.5 of the SmPC in order to amend posology recommendations, warnings and drug-drug interaction information regarding the co-administration with CYP3A4 inhibitors, P-gp inhibitors and CYP3A4 inducers based on final

results from the DDI study GP43162, listed as a category 3 study in the RMP, as well as results from the physiologically based pharmacokinetic (PBPK) analyses summarised in the PBPK Report 1120689. Study GP43162 is a phase 1, open-label, fixed-sequence study to evaluate the effect of a single dose of cyclosporine on the single dose pharmacokinetics of pralsetinib in healthy subjects. The RMP version 1.6 has also been submitted

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

5.3.29. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0046

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy and breast-feeding based on final results from study IMPAACT 2032 listed as a category 3 study in the RMP; this is a phase 4, prospective, open-label, non-randomised study to address PK and safety of remdesivir in pregnant women. The package leaflet is updated accordingly. The RMP version 5.2 has also been submitted

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

5.3.30. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0050

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to address the safety of remdesivir and its metabolites in patients with hepatic impairment and to update information on hepatic and coagulation laboratory abnormalities based on final results from study GS US 540 9014 (listed as category 3 study in the RMP): a phase 1 open-label, adaptive, single-dose study to evaluate the pharmacokinetics of remdesivir and its metabolite(s) in subjects with normal hepatic function and hepatic impairment, and on safety data from post-marketing and clinical trials experience. The package leaflet is updated accordingly. The RMP version 5.4 has also been submitted. In addition, the MAH took the opportunity submit Minor Linguistic Amendments (MLA) for Veklury

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

5.3.31. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/X/0038

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nathalie Gault

Scope: Extension application to add a new strength of 100 µg film-coated tablets in HDPE bottle. The RMP (version 10.1) is updated in accordance

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

5.3.32. Talazoparib - TALZENNA (CAP) - EMEA/H/C/004674/X/0015/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Grouped application consisting of: 1) Addition of a new strength of 0.1 mg hard capsules; 2)Extension of indication to add talazoparibin combination with enzalutamide for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC), based on final results from study C3441021 (TALAPRO-2) as well as supplemental data from study C3441006 (TALAPRO-1). Study C3441021 (TALAPRO-2) is a randomised, double-blind, placebo-controlled, phase 3 study of talazoparib in combination with enzalutamide in mCRPC, while study C3441006 (TALAPRO-1) is a phase 2, open-label, response rate study of talazoparib in men with DNA repair defects and mCRPC who previously received taxane-based chemotherapy and progressed on at least one novel hormonal agent. As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.5, 4.7, 4.8, 5.1, 5.2, 6.1, 6.5, 8 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.33. Thalidomide - THALIDOMIDE BMS (CAP) - EMEA/H/C/000823/II/0076

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 4.4 of the SmPC, Annex IID and Article 127a and the tools/documents included in the Educational Healthcare Professional Kit, in order to harmonise the terminology utilised in the RMP and product information documents relating to the safety concern of teratogenicity and its risk minimisation measure of the Pregnancy Prevention Plan (PPP) across the 3 immunomodulatory imide drugs (IMiDs). These proposed changes will only have a limited impact on the National Competent Authority (NCA)-approved content/text of the educational materials, and the key messages to the HCP and patients. Furthermore, the regulatory obligations regarding the PPP will not be impacted. The MAH is also taking the opportunity to update the RMP with PASS Protocol milestones, and to make some editorial changes in the labelling. The updated RMP version 20 was provided

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

5.3.34. Tirzepatide - MOUNJARO (CAP) - EMEA/H/C/005620/II/0007

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include chronic weight management, including weight loss and weight maintenance, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial body mass index (BMI) of ≥ 30 kg/m2 (obesity), or ≥ 27 kg/m2 to < 30 kg/m2 (overweight) in the presence of at least one weight-related comorbid condition, based on a global, pivotal phase 3 study I8F-MC-GPHK (SURMOUNT-1) and five supportive phase 3 studies (SURPASS-1 to -5) in participants with T2DM and BMI ≥ 27 kg/m2. SURMOUNT-1 is a phase 3, randomised, double-blind, placebo-controlled trial to investigate the efficacy and safety of tirzepatide once weekly in participants without type 2 diabetes who have obesity or are overweight with weight related comorbidities. As a

consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.35. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/II/0177/G

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Grouped application consisting of: 1) Extension of indication to include Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose concentrate for dispersion for injection and Comirnaty Original/Omicron BA.4-5 (15/15 micrograms)/dose dispersion for injection for use as primary vaccination course against COVID-19 in children aged 5 to 11 years and in individuals 12 years of age and older, respectively, based on interim results from studies C4591044 and C4591048. Study C4591044 is an interventional, randomised, active-controlled, phase 2/3 study to investigate the safety, tolerability, and immunogenicity of bivalent BNT162b RNA-based vaccine candidates as a booster dose in COVID-19 vaccine–experienced healthy individuals, while study C4591048 is a phase 1/2/3 master study to investigate the safety, tolerability, and immunogenicity of a bivalent BNT162b2 RNA-based vaccine candidate. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 9.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information; 2) To change the ATC Code of tozinameran, riltozinameran and famtozinameran from J07BX03 to J07BN01

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

5.3.36. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/X/0176

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Extension application to add a new strength of 1.5/1.5 µg (tozinameran, famtozinameran) for active immunisation in infants and children between 6 months to 4 years of age

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

5.3.37. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/X/0180

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Extension application to add a new strength of 5/5 µg (tozinameran, famtozinameran) dispersion for injection for active immunisation for children aged 5 to 11 years of age

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

5.3.38. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/II/0031

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update safety, efficacy and pharmacokinetic information based on data from study DS8201-A-U301 and study DS8201-A-U302. Study U301 was a Phase 3, randomised, 2-arm, open-label, multicenter study designed to compare the safety and efficacy of T-DXd vs TPC in HER2-positive, unresectable and/or metastatic BC subjects who were resistant or refractory to T-DM1. Study U302 was a Phase 3, multicenter, randomised, open-label, 2-arm, active-controlled study in subjects with unresectable and/or metastatic HER2-positive (IHC 3+ or ISH-positive) BC previously treated with trastuzumab plus taxane in the advanced/metastatic setting or who had progressed within 6 months after neoadjuvant or adjuvant treatment involving a regimen including trastuzumab plus taxane. The package leaflet and Annex II are updated accordingly. The updated RMP version 4.1 has also been submitted

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

5.3.39. Vonicog alfa - VEYVONDI (CAP) - EMEA/H/C/004454/II/0030

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include prophylactic treatment to prevent or reduce the frequency of bleeding episodes based on final results from study 071301 and interim results from study SHP677-304. Study 071301 is a prospective, phase 3, open-label, international multicenter study on efficacy and safety of prophylaxis with rVWF in severe von Willebrand disease; while study SHP677-304 is a phase 3B, prospective, open-label, uncontrolled, multicenter study on long term safety and efficacy of rVWF in paediatric and adult subjects with severe von Willebrand disease. As a consequence, sections 4.1, 4.2, 4.4, 5.1, 5.2, 6.2 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted

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

5.3.40. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/II/0014

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include zanubrutinib in combination with obinutuzumab treatment of adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic treatments for BRUKINSA, based on results from studies BGB-3111-212 and BGB-3111-GA101-001. BGB-3111-212 is an ongoing international, Phase 2, open-label, randomised (2:1), active control study of zanubrutinib plus obinutuzumab (Arm A) versus obinutuzumab monotherapy (Arm B) in patients with R/R FL. The primary efficacy endpoint is overall response rate (ORR); while BGB-3111-GA101-001 is a Phase 1b Study to Assess Safety, Tolerability and Antitumor Activity of the Combination of BGB-3111 with Obinutuzumab in Subjects with B-Cell Lymphoid Malignanciesa. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated.

The package leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC

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. Acalabrutinib - CALQUENCE (CAP) - PSUSA/00010887/202210

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Aclidinium bromide, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP); DUAKLIR GENUAIR (CAP) - PSUSA/00010307/202211

Applicant: Covis Pharma Europe B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alpelisib - PIQRAY (CAP) - PSUSA/00010871/202211

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Amivantamab - RYBREVANT (CAP) - PSUSA/00010977/202211

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Artenimol, piperaquine tetraphosphate - EURARTESIM (CAP) - PSUSA/00001069/202210

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Benralizumab - FASENRA (CAP) - PSUSA/00010661/202211

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Capmatinib - TABRECTA (CAP) - PSUSA/00011022/202211

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Cefiderocol - FETCROJA (CAP) - PSUSA/00010849/202211

Applicant: Shionogi B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Ceritinib - ZYKADIA (CAP) - PSUSA/00010372/202210

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - PSUSA/00010449/202211

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Valentina Di Giovanni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Crizanlizumab - ADAKVEO[8] (CAP) - PSUSA/00010888/202211

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.12. Daratumumab - DARZALEX (CAP) - PSUSA/00010498/202211

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Dinutuximab beta - QARZIBA (CAP) - PSUSA/00010597/202211

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Drospirenone, estetrol - DROVELIS (CAP); LYDISILKA (CAP) - PSUSA/00010938/202211

Applicant: Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.) (Drovelis), Estetra SRL (Lydisilka)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Emicizumab - HEMLIBRA (CAP) - PSUSA/00010668/202211

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[8] See EMA communication on revocation of authorisation for sickle cell disease medicine Adakveo

6.1.16. Givosiran - GIVLAARI (CAP) - PSUSA/00010839/202211

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Glasdegib - DAURISMO (CAP) - PSUSA/00010859/202211

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Hepatitis B surface antigen, CpG 1018 adjuvant - HEPLISAV B (CAP) - PSUSA/00010919/202211

Applicant: Dynavax GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Hydrocortisone[9] - EFMODY (CAP); PLENADREN (CAP) - PSUSA/00009176/202211

Applicant: Diurnal Europe BV (Efmody), Takeda Pharmaceuticals International AG Ireland Branch (Plenadren)

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Ibrutinib - IMBRUVICA (CAP) - PSUSA/00010301/202211

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Insulin glargine, lixisenatide - SULIQUA (CAP) - PSUSA/00010577/202211

Applicant: Sanofi Winthrop Industrie

[9] For centrally authorised products for adrenal insufficiency, congenital adrenal hyperplasia, modified-release formulations

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Ixazomib - NINLARO (CAP) - PSUSA/00010535/202211

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Linzagolix choline - YSELTY (CAP) - PSUSA/00010998/202211

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Lonafarnib - ZOKINVY (CAP) - PSUSA/00011005/202211

Applicant: EigerBio Europe Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Lumasiran - OXLUMO (CAP) - PSUSA/00010884/202211

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Nintedanib[10] - VARGATEF (CAP) - PSUSA/00010318/202210

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Georgia Gkegka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[10] Oncology indications only

6.1.27. Ocriplasmin - JETREA (CAP) - PSUSA/00010122/202210

Applicant: Inceptua AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Ozanimod - ZEPOSIA (CAP) - PSUSA/00010852/202211

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Padeliporfin - TOOKAD (CAP) - PSUSA/00010654/202211

Applicant: STEBA Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - PSUSA/00010501/202211

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Pegcetacoplan - ASPAVELI (CAP) - PSUSA/00010974/202211

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Potassium citrate, potassium hydrogen carbonate - SIBNAYAL (CAP) - PSUSA/00010932/202210

Applicant: Advicenne

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Remdesivir - VEKLURY (CAP) - PSUSA/00010840/202211

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Ripretinib - QINLOCK (CAP) - PSUSA/00010962/202211

Applicant: Deciphera Pharmaceuticals (Netherlands) B.V.

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Rituximab - BLITZIMA (CAP); MABTHERA (CAP); RIXATHON (CAP); RIXIMYO (CAP); RUXIENCE (CAP); TRUXIMA (CAP) - PSUSA/00002652/202211

Applicant: Roche Registration GmbH (MabThera), Sandoz GmbH (Rixathon, Riximyo), Pfizer Europe MA EEIG (Ruxience), Celltrion Healthcare Hungary Kft. (Blitzima, Truxima)

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Rurioctocog alfa pegol - ADYNOVI (CAP) - PSUSA/00010663/202211

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Selpercatinib - RETSEVMO (CAP) - PSUSA/00010917/202211

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Setmelanotide - IMCIVREE (CAP) - PSUSA/00010941/202211

Applicant: Rhythm Pharmaceuticals Netherlands B.V.,

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Stiripentol - DIACOMIT (CAP) - PSUSA/00002789/202211

Applicant: BIOCODEX

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Susoctocog alfa - OBIZUR (CAP) - PSUSA/00010458/202211

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Tirzepatide - MOUNJARO (CAP) - PSUSA/00011019/202211

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Tixagevimab, cilgavimab - EVUSHELD (CAP) - PSUSA/00010992/202211

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/202211

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Vestronidase alfa - MEPSEVII (CAP) - PSUSA/00010709/202211

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Volanesorsen - WAYLIVRA (CAP) - PSUSA/00010762/202211

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Zanubrutinib - BRUKINSA (CAP) - PSUSA/00010960/202211

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Deferasirox - DEFERASIROX ACCORD (CAP); DEFERASIROX MYLAN (CAP); EXJADE (CAP); NAP - PSUSA/00000939/202210

Applicants: Accord Healthcare S.L.U. (Deferasirox Accord), Mylan Pharmaceuticals Limited (Deferasirox Mylan), Novartis Europharm Limited (EXJADE), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Doxorubicin - CAELYX PEGYLATED LIPOSOMAL (CAP); CELDOXOME PEGYLATED LIPOSOMAL (CAP); MYOCET LIPOSOMAL (CAP); ZOLSKETIL PEGYLATED LIPOSOMAL (CAP); NAP - PSUSA/00001172/202211

Applicants: Baxter Holding B.V. (Caelyx pegylated liposomal), YES Pharmaceutical Development Services GmbH (Celdoxome pegylated liposomal), Teva B.V. (Myocet liposomal), Accord Healthcare S.L.U. (Zolsketil pegylated liposomal), various

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Tadalafil - ADCIRCA (CAP); CIALIS (CAP); TADALAFIL LILLY (CAP); NAP - PSUSA/00002841/202210

Applicants: Eli Lilly Nederland B.V. (Adcirca, Cialis, Tadalafil Lilly), various

PRAC Rapporteur: Maria del Pilar Rayon

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. Acitretin (NAP) - PSUSA/00000051/202210

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Atovaquone, proguanil (NAP) - PSUSA/00000266/202210

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Clevidipine (NAP) - PSUSA/00010288/202211

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Drospirenone (NAP) - PSUSA/00010853/202211

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Epinastine (NAP) - PSUSA/00001231/202210

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Ezetimibe (NAP) - PSUSA/00001346/202210

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Human coagulation factor VII (NAP) - PSUSA/00001619/202210

Applicant(s): various

PRAC Lead: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Isoflurane (NAP) - PSUSA/00001786/202210

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Lenograstim (NAP) - PSUSA/00001839/202210

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Morphine (NAP), morphine, cyclizine (NAP) - PSUSA/00010549/202210

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Rubidium (^{82}Rb) chloride (NAP) - PSUSA/00010806/202210

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Tixocortol (NAP), chlorhexidine gluconate, tixocortol pivalate (NAP) - PSUSA/00010333/202211

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Valsartan, rosuvastatin (NAP) - PSUSA/00010735/202210

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

None

6.5. Variation procedure(s) resulting from PSUSA evaluation

None

6.6. Expedited summary safety reviews[11]

None

[11] 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

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[12]

7.1.1. Axicabtagene ciloleucel - Yescarta (CAP) - EMEA/H/C/PSA/S/0102.1

Applicant: Kite Pharma EU B.V., ATMP[13]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Substantial amendment to a protocol for a long-term, non-interventional study of recipients of Yescarta for treatment of relapsed or refractory Diffuse Large B-cell Lymphoma and Primary Mediastinal B-cell Lymphoma [MAH's response to PSA/S/0102]

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

7.1.2. Valproate[14] (NAP) - EMEA/H/N/PSP/J/0075.11

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Responses to the request to supplementary information (RSI) of the third interim report and updated protocol (version 11) for drug utilisation study (DUS) extension (DUS ext.) to assess the effectiveness of the new risk minimisation measures and to further characterise the prescribing patterns for valproate and related substances [MAH's response to PSP/J/0075.10]

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

7.1.3. Valproate[15] (NAP) - EMEA/H/N/PSP/J/0075.12

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Responses to the request to supplementary information (RSI) of the fourth interim report and Statistical Analysis Plan for drug utilisation study (DUS) extension (DUS ext.) to assess the effectiveness of the new risk minimisation measures and to further characterise the prescribing patterns for valproate and related substances [MAH's response to PSP/J/0075.9]

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

[12] In accordance with Article 107n of Directive 2001/83/EC
[13] Advanced therapy medicinal product
[14] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium
[15] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[16]

7.2.1. Abaloparatide - ELADYNOS (CAP) - EMEA/H/C/005928/MEA 001

Applicant: Radius Health (Ireland) Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of a protocol for an European non-interventional PASS to assess serious cardiovascular events of MI, stroke, all-cause and cardiovascular mortality, and arrhythmias for abaloparatide

Action: For adoption of advice to CHMP

7.2.2. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 002.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 002.1[protocol for study B7451084: an active surveillance study to monitor the real-world safety of abrocitinib among patients with atopic dermatitis (AD) in the EU. The objective of the study is to estimate the incidence rates of safety endpoints of interest among AD patients receiving abrocitinib and AD patients receiving appropriate systemic treatments including dupilumab for AD in a real-world setting] as per the request to supplementary information (RSI) as adopted in January 2023

Action: For adoption of advice to CHMP

7.2.3. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 003.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 003.1 [protocol for study B7451085: a drug utilisation study to evaluate the effectiveness of risk minimisation measures (RMMs) for abrocitinib in the EU using electronic healthcare data. The study objectives will be to evaluate indicators of HCP's adherence to the risk minimisation measures in accordance with the abrocitinib SmPC and prescriber brochure] as per the request to supplementary information (RSI) adopted in January 2023

Action: For adoption of advice to CHMP

7.2.4. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/MEA 002.7

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: MAH's response to MEA 002.6 [protocol amendment to include a cohort to Study D8220C00008: phase 3b, multicentre, open-label, single-arm in subjects with chronic

[16] 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

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 February 2023

Action: For adoption of advice to CHMP

7.2.5. Anifrolumab - SAPHNELO (CAP) - EMEA/H/C/004975/MEA 001.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study D3461R00028: a multiple database study of the use (and safety) of anifrolumab in women with systemic lupus erythemathosus (SLE) during pregnancy

Action: For adoption of advice to CHMP

7.2.6. Avalglucosidase alfa - NEXVIADYME (CAP) - EMEA/H/C/005501/MEA 007.1

Applicant: Sanofi B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 007 [Protocol for study OBS17445 (listed as category 3 study in the RMP): a PASS to assess long term safety in patients with Pompe disease treated with avalglucosidase alfa in the commercial setting] as per request for supplementary information (RSI) adopted in January 2023

Action: For adoption of advice to CHMP

7.2.7. Avatrombopag - DOPTELET (CAP) - EMEA/H/C/004722/MEA 003.3

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Monica Martinez Redondo

Scope: MAH's response to MEA 003.2 [feasibility assessment for a study to further characterise the long-term safety profile of avatrombopag in patients with primary chronic immune thrombocytopenia in European patient registers and electronic healthcare databases as requested in the conclusions of variation II/0004/G finalised in December 2020] as per the request for supplementary information (RSI) adopted October 2022

Action: For adoption of advice to CHMP

7.2.8. Cipaglucosidase alfa - POMBILITI (CAP) - EMEA/H/C/005703/MEA 001

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Mari Thorn

Scope: Submission of a protocol for study POM-005 (non-imposed/non-interventional, listed as category 3 in the RMP): a global prospective observational registry of patients with pompe disease

Action: For adoption of advice to CHMP

7.2.9. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/MEA 003.3

Applicant: Merck Europe B.V.

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: MAH's responses to MEA 003.2 [Amendment to a previously agreed protocol for study MS700568-0004: Pregnancy outcomes in women exposed to oral cladribine: a multi-country cohort database study – CLEAR] as per the request for supplementary information (RSI) adopted in February 2023

Action: For adoption of advice to CHMP

7.2.10. Coronavirus (COVID-19) vaccine (B.1.351 variant, prefusion Spike delta TM protein, recombinant) - VIDPREVTYN BETA (CAP) - EMEA/H/C/005754/MEA 002.1

Applicant: Sanofi Pasteur

PRAC Rapporteur: Jana Lukacisinova

Scope: MAH's response to MEA 002 [Submission of a protocol for study VAT 00007: Post-authorisation, observational study to assess the safety of VidPrevtyn Beta using routinely collected secondary data in Europe through VAC4EU. A non-interventional PASS to assess the occurrence of pre-specified AESIs and safety concerns following administration of VidPrevtyn Beta as a booster dose in a real-world setting as per the request for supplementary information (RSI) adopted in February 2023

Action: For adoption of advice to CHMP

7.2.11. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/MEA 046.7

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 046.6 [Substantial amendment to a protocol previously endorsed in November 2017 for study CC-5013-MCL-005 to further investigate and characterise the association of lenalidomide and tumour flare reaction (TFR)/high tumour burden following the extension of indication for the treatment of adult patients with relapsed and/or refractory mantle cell lymphoma (RRMCL)] as per the request for supplementary information (RSI) adopted in February 2032

Action: For adoption of advice to CHMP

7.2.12. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/MEA 003.3

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 003.2[Submission of an updated study protocol (version 1.0) for study A4250-019 (listed as a category 3 study in the RMP): prospective registry-based study of the long-term safety of odevixibat in patients with progressive familial intrahepatic cholestasis (PFIC) to collect safety data on hepatotoxicity, diarrhoea, fat-soluble vitamins and fat-soluble nutrients in patients treated with odevixibat] as per request

for supplementary information (RSI) adopted in February 2023

Action: For adoption of advice to CHMP

7.2.13. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 005.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 005 [protocol for study IM0471037: a PASS titled 'Long-term real-world safety of ozanimod – A PASS in patients diagnosed with ulcerative colitis'. This study is a category 3 study (required additional pharmacovigilance activity - UC indication) listed in the RMP version 3.0] as per the request for supplementary information (RSI) adopted in September 2022

Action: For adoption of advice to CHMP

7.2.14. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 009

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study P23-653 (non-imposed/non-interventional): Pregnancy Exposure and Outcomes for Women with Crohn's Disease Treated with Risankizumab. A comparative cohort study to describe risankizumab exposure in pregnant patients with Crohn's disease, and compare pregnancy and infant outcomes to pregnant patients with Crohn's disease who were treated with alternative therapies (e.g., biologics). In addition, descriptive analyses of pregnancy outcomes in patients with Crohn's disease without exposure to any treatments under investigation will also be conducted

Action: For adoption of advice to CHMP

7.2.15. Spesolimab - SPEVIGO (CAP) - EMEA/H/C/005874/MEA 003

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nathalie Gault

Scope: Protocol for study 1368-0128 (Non-imposed/Non-interventional): a 5-year active surveillance, PASS to characterise the safety of spesolimab for flare treatment in patients with generalized pustular psoriasis (GPP). Objectives: To evaluate the risks serious or opportunistic infections, systemic hypersensitivity reaction, malignancy, and peripheral neuropathy in adult patients (aged ≥18 years) experiencing a GPP flare who are treated with spesolimab or other treatments in the routine clinical care setting

Action: For adoption of advice to CHMP

7.2.16. Tezepelumab - TEZSPIRE (CAP) - EMEA/H/C/005588/MEA 001

Applicant: AstraZeneca AB

PRAC Rapporteur: Eva Jirsová

Scope: Protocol for study D5180R00010 (TREATY): A Non-Interventional Multi-Database PASS to Assess Pregnancy-Related Safety Data from Women with Severe Asthma Exposed to Tezepelumab

Action: For adoption of advice to CHMP

7.2.17. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 003.4

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 003.2 [Amendment to a previously agreed protocol for study P19-150: a long-term PASS of upadacitinib use in rheumatoid arthritis (RA) patients in Europe to evaluate the safety of upadacitinib among patients with RA receiving routine clinical care to include additional study outcomes of bone fractures and add further clarification that the malignancy outcomes will be stratified for malignancies excluding non-melanoma skin cancer (NMSC) and NMSC, separately (RMP version 6.2)] as per request for supplementary information (RSI) adopted in January 2023

Action: For adoption of advice to CHMP

7.2.18. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 004.4

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 004.2 [Amendment to a previously agreed protocol for study P19-141: a long-term PASS of upadacitinib use in rheumatoid arthritis (RA) patients in the US in order to: 1) compare the incidence of malignancy, non-melanoma skin cancer (NMSC), major adverse cardiovascular events (MACE), venous thromboembolism (VTE) and serious infection events in adults with RA who receive upadacitinib in the course of routine clinical care relative to those who receive biologic therapy for the treatment of RA; 2) describe the incidence rates of herpes zoster, opportunistic infections and evidence of drug-induced liver injury (DILI); 3) describe the incidence of the above outcomes in very elderly patients (aged $\geqslant$ 75 years); 4) characterise VTE clinical risk factors and baseline biomarkers in a sub-study of new initiators of upadacitinib and comparator biologic therapies] as per request for supplementary information (RSI) adopted in January 2023

Action: For adoption of advice to CHMP

7.2.19. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 012.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 012.2 [protocol for study P21-825: an evaluation of the effectiveness of additional risk minimisation measures for upadacitinib in the treatment of atopic dermatitis] as per the request for supplementary information (RSI) adopted in January 2023

Action: For adoption of advice to CHMP

7.2.20. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 013.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 013.2 [revised protocol for study P20-390: a cohort study of long-term safety of upadacitinib in the treatment of atopic dermatitis in Denmark and Sweden] as per request for supplementary information (RSI) adopted in December 2022

Action: For adoption of advice to CHMP

7.2.21. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 016.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 016 [Protocol for study P23-479: a drug utilisation study for evaluation of the effectiveness of additional risk minimisation measures for upadacitinib in the treatment of ulcerative colitis in Sweden and Denmark] as per request for supplementary information (RSI) adopted in January 2023

Action: For adoption of advice to CHMP

7.2.22. Valoctocogene roxaparvovec - ROCTAVIAN (CAP) - EMEA/H/C/005830/MEA 005

Applicant: BioMarin International Limited, ATMP[17]

PRAC Rapporteur: Menno van der Elst

Scope: Protocol of a survey of haematologists to assess the effectiveness of the additional risk minimisation measures (aRMMs) for ROCTAVIAN (valoctocogene roxaparvovec)

Action: For adoption of advice to CAT and CHMP

7.2.23. Voclosporin - LUPKYNIS (CAP) - EMEA/H/C/005256/MEA 002

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Protocol for study 348-201-00021 (Non-imposed/Non-interventional, listed as category 3 study in the RMP): Observational PASS in Europe to further characterise and quantify long-term safety profile with respect to neurotoxicity, chronic nephrotoxicity, and malignancy with use of voclosporin

Action: For adoption of advice to CHMP

[17] Advanced therapy medicinal product

7.3. Results of PASS imposed in the marketing authorisation(s)[18]

7.3.1. Valproate[19] (NAP) - EMEA/H/N/PSR/J/0043

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Final study report for a retrospective observational study to investigate the association between paternal exposure to valproate and the risk of congenital anomalies and neurodevelopmental disorders including autism in offspring

Action: For adoption of revised list of questions (LoQ)/timetable

7.4. Results of PASS non-imposed in the marketing authorisation(s)[20]

7.4.1. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0039/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final reports from studies I4V-MC-B016 and I4V-MC-B011 listed as category 3 non-interventional PASS studies in the RMP. B016 is a drug utilisation study for the assessment of off-label use of baricitinib in the paediatric population in the United Kingdom. B011 is a retrospective cohort study to assess the safety of baricitinib compared with other therapies used in the treatment of rheumatoid arthritis in Nordic countries. The RMP version 19.1 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.2. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/II/0033

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study F-FR-60000-001 (CASSIOPE) listed as a category 3 study in the RMP. This is a prospective, non-imposed and non-interventional study of Cabozantinib tablets in adults with advanced renal cell carcinoma (RCC) following prior vascular endothelial growth factor (VEGF)-targeted therapy. The RMP version 7.0 has also been submitted

Action: For adoption of PRAC Assessment Report

[18] In accordance with Article 107p-q of Directive 2001/83/EC
[19] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium
[20] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

7.4.3. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - EMEA/H/C/005737/II/0071/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped application consisting of: 1) Submission of the final study report of a clinical TTS characterization study listed as a category 3 study in the RMP. This is a Test Pre- and Post-Vaccination Serum Across All Populations Using Clinical Samples From Ad26-based Company Vaccine Studies Other Than Ad26.COV2.S; 2) Submission of the Addendum to final CSR of the study VAC31518COV2001 listed as a category 3 study in the RMP. This is a randomised, double-blind, placebo-controlled Phase 2a study to evaluate a range of dose levels and vaccination intervals of Ad26.COV2.S in healthy adults aged 18 to 55 years, and adults aged 65 years and older. The RMP version 6.1 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.4. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0091

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study D8111R00020 listed as a category 3 study in the RMP. This is a systematic literature review for studies evaluating adverse events of Vaxzervria in patients taking immunosuppressant medications and/or with primary immunodeficiency

Action: For adoption of PRAC Assessment Report

7.4.5. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/II/0144

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final report from the Human Factors Study (007-HFE-009035), listed as a category 3 study in the RMP; this is a non-interventional study to assess the effectiveness of a training video to mitigate potential medication errors during the reconstitution and dosing of the dabigatran etexilate paediatric oral solution

Action: For adoption of PRAC Assessment Report

7.4.6. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/WS2483/0045; ROTEAS (CAP) - EMEA/H/C/004339/WS2483/0032

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Nathalie Gault

Scope: Submission of the final report from DSE-EDO-04-14-EU (Non-Interventional Study on Edoxaban Treatment in Routine Clinical Practice for Patients with Non-Valvular Atrial Fibrillation, ETNA-AF Europe), listed as a category 3 study in the RMP (MEA 006). This is a

multicentre, prospective, non-interventional, observational PASS. The RMP version 15.1 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.7. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0126

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report from study CC-5013-MDS-010 listed as an obligation in the Annex II of the product information. This is a prospective non-interventional PASS, designed as a disease registry of patients with transfusion dependent IPSS low or intermediate-1-risk myelodysplastic syndromes (MDS) and isolated del(5q). Section D of the Annex II and the RMP (version 39) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. Piperaquine tetraphosphate, artenimol - EURARTESIM (CAP) - EMEA/H/C/001199/II/0040/G

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Martin Huber

Scope: Grouped variation consisting of: 1) Submission of the final report from the effectiveness evaluation survey for Eurartesim (protocol no. 3366) (listed as a category 3 study in the RMP): an European multi-centre online survey to assess physician understanding of the revised edition of the educational material. Consequential changes to RMP version 16.1 have been implemented; 2) Submission of an updated RMP version 16.1 in order to delete "severe malaria" as missing information from the list of safety specifications

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.15

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

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

Action: For adoption of advice to CHMP

7.5.2. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/ANX 010.8

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to ANX 010.7 [Interim report 2 for study DUT0008: non-interventional PASS to investigate drug utilisation and safety monitoring patterns for Lemtrada (alemtuzumab)] as per the request for supplementary information (RSI) adopted in February 2023

Action: For adoption of advice to CHMP

7.5.3. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/MEA 050.5

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Third interim report for study PASS C18477-ONC-50025: a post-authorisation long term safety cohort study in acute promyelocytic leukaemia (APL) patients treated with Trisenox (arsenic trioxide) to assess the long-term safety of all-trans retinoic acid (ATRA) + arsenic trioxide (ATO) in newly-diagnosed low to intermediate risk APL patients in a real-world clinical practice setting

Action: For adoption of advice to CHMP

7.5.4. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/MEA 002.5

Applicant: Merck Europe B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Fourth yearly progress update report for study MS100070-0031 (listed as a category 3 study in the RMP): a non-interventional cohort study to assess characteristics and management of patients with Merkel cell carcinoma (MCC) in Germany

Action: For adoption of advice to CHMP

7.5.5. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/ANX 004.4

Applicant: Orchard Therapeutics (Netherlands) B.V., ATMP[21]

PRAC Rapporteur: Menno van der Elst

Scope: Third interim report for study GSK2696273 – an adenosine deaminase severe combined immunodeficiency (ADA-SCID) registry for patients treated with Strimvelis gene therapy: a long-term prospective, non-interventional follow-up of safety and effectiveness

Action: For adoption of advice to CAT and CHMP

[21] Advanced therapy medicinal product

7.5.6. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/MEA 004.3

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Interim report for study 215162 (listed as a category 3 study in the RMP): a prospective observational cohort study to monitor for hepatotoxicity and regimen discontinuation due to liver related adverse events among patients initiating cabotegravir-containing antiretroviral regimen

Action: For adoption of advice to CHMP

7.5.7. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/ANX 002

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Interim report for a drug utilisation study (DUS): Drug Utilisation, Adherence, Effectiveness and Resistance: A Prospective Observational Cohort Study in People Living with HIV (PLWH) initiating ARV regimen CAB+RPV LA in Collaboration with EuroSIDA

Action: For adoption of advice to CHMP

7.5.8. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 114

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: First progress report for study No. D8111R00010; ATTEST (Association of the risk for Thrombotic Thrombocytopenia Syndrome and Exposure To COVID-19 vaccines) is a category 3 PASS study with the objective to evaluate an association between COVID-19 vaccine exposure and thromboembolic events occurring with thrombocytopenia (thrombotic thrombocytopenia syndrome; TTS)

Action: For adoption of advice to CHMP

7.5.9. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 007.14

Applicant: Hexal AG

PRAC Rapporteur: Menno van der Elst

Scope: Twelfth annual report for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation

Action: For adoption of advice to CHMP

7.5.10. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.14

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Twelfth annual report for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation

Action: For adoption of advice to CHMP

7.5.11. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 007.4

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 007.3 [Second interim report for study TEG4005: a pregnancy surveillance programme of infants and women exposed to Tegsedi (inotersen) during pregnancy] as per request for supplementary information (RSI) adopted in February 2023

Action: For adoption of advice to CHMP

7.5.12. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/MEA 001.3

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: MAH's response to MEA 001.2 [Interim report for a PASS to characterise the safety of allogeneic haematopoietic stem cell transplantation (HSCT) in patients with cutaneous T-cell lymphoma (CTCL) treated with mogamulizumab] as per request for supplementary information (RSI) adopted in February 2023

Action: For adoption of advice to CHMP

7.5.13. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 003.2

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Second interim report for study COMB157G2399 (ALITHIOS) study (listed as a category 3 study in the RMP): an open-label, single arm, multicentre extension study evaluating long-term safety, tolerability and effectiveness of ofatumumab in subjects with relapsing multiple sclerosis

Action: For adoption of advice to CHMP

7.5.14. Rilpivirine - REKAMBYS (CAP) - EMEA/H/C/005060/ANX 002

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: First annual interim report for the non-interventional PASS drug utilisation study (DUS) (listed as category 1 study in the RMP): 'Drug Utilization, Adherence, Effectiveness and Resistance: A Prospective Observational Cohort Study in People living with HIV (PLWH) initiating ARV regimen CAB+RPV LA in Collaboration with EuroSIDA'

Action: For adoption of advice to CHMP

7.5.15. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 001.9

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nathalie Gault

Scope: Interim report for study EXPOSURE: an observational cohort study of pulmonary arterial hypertension (PAH) patients newly treated with either Uptravi (selexipag) or any other PAH-specific therapy, in clinical practice

Action: For adoption of advice to CHMP

7.5.16. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 008.6

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Second interim report for study A3921312 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA)

Action: For adoption of advice to CHMP

7.5.17. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 009.6

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Second interim report for study A3921314: (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Swedish (ARTIS) register

Action: For adoption of advice to CHMP

7.5.18. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 010.6

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Second interim report for study A3921316 (listed as a category 3 study in the RMP):

a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Spanish registry of adverse events of biological therapies and biosimilars in rheumatoid diseases (BIOBADASER)

Action: For adoption of advice to CHMP

7.5.19. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 011.6

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Second interim report for study A3921317: (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)

Action: For adoption of advice to CHMP

7.5.20. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.9

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study C4591010: a post-approval active surveillance safety study to monitor real-world safety of Comirnaty (tozinameran) vaccine in the EU

Action: For adoption of advice to CHMP

7.5.21. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 003.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Annual progress report for study P19-150 (EUPAS39217): a long-term PASS of upadacitinib use in rheumatoid arthritis (RA) patients in Europe to evaluate the safety of upadacitinib among patients with RA receiving routine clinical care

Action: For adoption of advice to CHMP

7.5.22. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 004.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Annual progress report for study P19-141 (EUPAS39194): a long-term PASS of upadacitinib use in rheumatoid arthritis (RA) patients in the US in order to: 1) compare the incidence of malignancy, non-melanoma skin cancer (NMSC), major adverse cardiovascular events (MACE), venous thromboembolism (VTE) and serious infection events in adults with

RA who receive upadacitinib in the course of routine clinical care relative to those who receive biologic therapy for the treatment of RA; 2) describe the incidence rates of herpes zoster, opportunistic infections and evidence of drug-induced liver injury (DILI); 3) describe the incidence of the above outcomes in very elderly patients (aged ⩾ 75 years); 4) characterise VTE clinical risk factors and baseline biomarkers in a sub-study of new initiators of upadacitinib and comparator biologic therapies

Action: For adoption of advice to CHMP

7.5.23. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 005.2

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Annual progress report for study P20-199 (EUPAS39211): a drug utilisation study (DUS) to evaluate the effectiveness of the additional risk minimisation measures (aRMM) in place to describe the baseline characteristics of new users of upadacitinib, and in a similar manner, to describe new users of a biological disease-modifying antirheumatic drugs (bDMARD) for comparison

Action: For adoption of advice to CHMP

7.5.24. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.16

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Fifth interval safety registry for study CNTO1275PSO4056: an observational PASS of ustekinumab in the treatment of paediatric patients aged 12 years and older with moderate to severe plaque psoriasis (adolescent registry)

Action: For adoption of advice to CHMP

7.6. Others

None

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/S/0045 (without RMP)

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Clofarabine - EVOLTRA (CAP) - EMEA/H/C/000613/S/0078 (without RMP)

Applicant: Sanofi B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/003922/S/0031 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

None

8.2.1. Belantamab mafodotin - BLENREP (CAP) - EMEA/H/C/004935/R/0017 (with RMP)

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Crizanlizumab - ADAKVEO (CAP) - EMEA/H/C/004874/R/0014 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jo Robays

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Dengue tetravalent vaccine (live, attenuated) - DENGVAXIA (CAP) - EMEA/H/C/004171/R/0027 (without RMP)

Applicant: Sanofi Pasteur

PRAC Rapporteur: Sonja Hrabcik

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Lanadelumab - TAKHZYRO (CAP) - EMEA/H/C/004806/R/0035 (without RMP)

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Lenalidomide - LENALIDOMIDE ACCORD (CAP) - EMEA/H/C/004857/R/0021 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Lidocaine, prilocaine - FORTACIN (CAP) - EMEA/H/C/002693/R/0038 (without RMP)

Applicant: Recordati Ireland Ltd

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Mexiletine - NAMUSCLA (CAP) - EMEA/H/C/004584/R/0014 (without RMP)

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/R/0021 (without RMP)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Pegfilgrastim - PELMEG (CAP) - EMEA/H/C/004700/R/0025 (without RMP)

Applicant: Mundipharma Corporation (Ireland) Limited

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/R/0038 (with RMP)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Trastuzumab - OGIVRI (CAP) - EMEA/H/C/004916/R/0054 (without RMP)

Applicant: Viatris Limited

PRAC Rapporteur: Gabriele Maurer

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/R/0046 (without RMP)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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. 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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. PRAC drafting group on the risks of dependence and addiction of opioids - preparation of Stakeholder consultation

Action: For discussion

12.21.1. EMA medical term s simplifier - plain-language description of medical terms related to medicines use

Action: For discussion

13. Any other business

Next meeting on: 03-06 July 2023

14. Explanatory notes

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

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures

(Items 2 and 3 of the PRAC agenda)

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

Signals assessment and prioritisation

(Item 4 of the PRAC agenda)

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC agenda)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC agenda)

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC agenda)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC agenda)

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

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