28 August 2023
EMA/PRAC/307705/2023
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 28-31 August 2023

Chair: Sabine Straus – Vice-Chair: Martin Huber

28 August 2023, 10:30 – 19:30, via teleconference

29 August 2023, 08:30 – 19:30, via teleconference

30 August 2023, 08:30 – 19:30, via teleconference

31 August 2023, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

14 September 2023, 09:00 – 12:00, via teleconference

Note on access to documents

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

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

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 28-31 August 2023. See September 2023 PRAC minutes (to be published post October 2023 PRAC meeting).

1.2. Agenda of the meeting on 28-31 August 2023

Action: For adoption

1.3. Minutes of the previous meeting on 03-06 July 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. Pseudoephedrine (NAP); pseudoephedrine, acetylsalicylic acid (NAP); pseudoephedrine, acetylcysteine, paracetamol (NAP); pseudoephedrine, acrivastine (NAP); pseudoephedrine, ascorbic acid, paracetamol (NAP); pseudoephedrine, cetirizine (NAP); pseudoephedrine, ebastine (NAP); pseudoephedrine, guaifenesin (NAP); pseudoephedrine, ibuprofen (NAP); pseudoephedrine, chlorphenamine (NAP); pseudoephedrine, chlorphenamine, codeine (NAP); pseudoephedrine, chlorphenamine, dextromethorphan (NAP); pseudoephedrine, chlorphenamine, paracetamol (NAP); pseudoephedrine, chlorphenamine, dextromethorphan, paracetamol (NAP); pseudoephedrine, dextromethorphan (NAP); pseudoephedrine, dextromethorphan, paracetamol (NAP); pseudoephedrine, dextromethorphan, ascorbic acid, paracetamol (NAP); pseudoephedrine, dextromethorphan, guaifenesin, paracetamol (NAP); pseudoephedrine, dextromethorphan, guaifenesin, triprolidine (NAP); pseudoephedrine, dextromethorphan, triprolidine (NAP); pseudoephedrine, diphenhydramine, paracetamol (NAP); pseudoephedrine, doxylamine, paracetamol (NAP); pseudoephedrine, loratadine (NAP); pseudoephedrine, paracetamol (NAP); pseudoephedrine, paracetamol, pholcodine (NAP); pseudoephedrine, triprolidine (NAP); pseudoephedrine, triprolidine, guaifenesin (NAP); pseudoephedrine, triprolidine, paracetamol (NAP); pseudoephedrine, desloratadine - AERINAZE (CAP) – EMA/H/A-31/1526

Applicant(s): various

PRAC Rapporteur: Eva Jirsová; PRAC Co-rapporteur: Krõõt Aab

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 the list of experts for the ad hoc expert group meeting (AHEG)

3.3. Procedures for finalisation

3.3.1. 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 recommendation to CMDh

3.4. Re-examination procedures[1]

None

3.5. Others

None

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

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Amphotericin B (NAP)

Applicant: various

PRAC Rapporteur: to be appointed

Scope: Signal of hyperkalaemia

Action: For adoption of PRAC recommendation

EPITT 19966 – New signal

Lead Member State(s): ES

4.1.2. Avatrombopag – DOPTELET (CAP)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Monica Martinez Redondo

Scope: Signal of antiphospholipid syndrome

Action: For adoption of PRAC recommendation

EPITT 19954 – New signal

Lead Member State(s): ES

4.1.3. Cefotaxime (NAP)

Applicant: various

PRAC Rapporteur: to be appointed

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)

Action: For adoption of PRAC recommendation

EPITT 19960 – New signal

Lead Member State(s): AT

4.1.4. Cobimetinib – COTELLIC (CAP); Vemurafenib – ZELBORAF (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: to be appointed

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

Scope: Signal of aphthous ulcer, mouth ulceration, stomatitis

Action: For adoption of PRAC recommendation

EPITT 19961 – New signal

Lead Member State(s): SE

4.1.5. Minoxidil[3] (NAP)

Applicant: various

PRAC Rapporteur: to be appointed

Scope: Signal of hypertrichosis in children following accidental exposure via patients

Action: For adoption of PRAC recommendation

EPITT 19951 – New signal

Lead Member State(s): IE

4.1.6. Nivolumab – OPDIVO (CAP), OPDUALAG (CAP)

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

Scope: Signal of pancreatic failure

Action: For adoption of PRAC recommendation

EPITT 19955 – New signal

Lead Member State(s): DE

4.1.7. Osimertinib – TAGRISSO (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Signal of anaphylactic reaction

Action: For adoption of PRAC recommendation

EPITT 19959 – New signal

Lead Member State(s): NL

4.1.8. Palbociclib – IBRANCE (CAP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of rhabdomyolysis by interaction with statins

[3] Topical formulation(s) only

Action: For adoption of PRAC recommendation

EPITT 19963 – New signal

Lead Member State(s): DK

4.2. New signals detected from other sources

4.2.1. Ipilimumab – YERVOY (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Signal of coeliac disease

Action: For adoption of PRAC recommendation

EPITT 19958 – New signal

Lead Member State(s): NL

4.3. Signals follow-up and prioritisation

4.3.1. Acetazolamide (NAP)

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of choroidal effusion and choroidal detachment

Action: For adoption of PRAC recommendation

EPITT 19924 – follow up to April 2023

4.3.2. Megestrol (NAP)

Applicant(s): various

PRAC Rapporteur: Eamon O'Murchu

Scope: Signal of meningioma

Action: For adoption of PRAC recommendation

EPITT 19923 – follow up to April 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. Arpraziquantel - EMEA/H/W/004252

Scope: Treatment of schistosomiasis in children

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

5.1.2. Azacitidine - EMEA/H/C/006154

Scope: Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML)

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

5.1.3. Elranatamab - EMEA/H/C/005908, PRIME, Orphan

Applicant: Pfizer Europe MA EEIG

Scope: Treatment of adult patients with relapsed or refractory multiple myeloma

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

5.1.4. Eribulin - EMEA/H/C/006134

Scope: Treatment of breast cancer and liposarcoma

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

5.1.5. Exagamglogene autotemcel - EMEA/H/C/005763, PRIME, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited, ATMP

Scope: Treatment of transfusion-dependent β-thalassemia and sickle cell disease

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

5.1.6. Fidanacogene elaparvovec - EMEA/H/C/004774, PRIME, Orphan

Applicant: Pfizer Europe MA EEIG, ATMP

Scope: Treatment of severe and moderately severe haemophilia B

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

5.1.7. Germanium (^{68}Ge) chloride, gallium (^{68}Ga) chloride - EMEA/H/C/006053

Scope: Indicated for in vitro radiolabelling of specific carrier molecules to be used for positron emission tomography (PET) imaging

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

5.1.8. Ibuprofen - EMEA/H/C/006129

Scope: Treatment of a haemodynamically significant patent ductus arteriosus in preterm newborn infants less than 34 weeks of gestational age

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

5.1.9. Leriglitazone - EMEA/H/C/005757, Orphan

Applicant: Minoryx Therapeutics S.L.

Scope: Treatment of cerebral progression and myelopathy in male patients with adrenoleukodystrophy (ALD)

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

5.1.10. Momelotinib - EMEA/H/C/005768, Orphan

Applicant: Glaxosmithkline Trading Services Limited

Scope: Treatment of disease-related splenomegaly or symptoms and anaemia

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

5.1.11. Paclitaxel - EMEA/H/C/006173

Scope: Treatment of metastatic breast cancer

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

5.1.12. Ranibizumab - EMEA/H/C/006055

Scope: Treatment of neovascular age-related macular degeneration (AMD)

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

5.1.13. Rozanolixizumab - EMEA/H/C/005824, Orphan

Applicant: UCB Pharma

Scope: Treatment of generalised myasthenia gravis (gMG)

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

5.1.14. Tofersen - EMEA/H/C/005493, Orphan

Applicant: Biogen Netherlands B.V.

Scope: Treatment of adults with amyotrophic lateral sclerosis (ALS), associated with a mutation in the superoxide dismutase 1 (SOD1) gene

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

5.1.15. Ustekinumab - EMEA/H/C/006101

Scope: Treatment of plaque psoriasis, arthritis psoriatic, Crohn's Disease and ulcerative colitis

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

5.1.16. Zoonotic influenza vaccine (h5n1) (surface antigen, inactivated, adjuvanted) - EMEA/H/C/006375

Scope: Active immunisation against H5 subtype of Influenza A virus

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

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

5.2.1. Aclidinium - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/WS2548/0051; EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/WS2548/0052

Applicant: Covis Pharma Europe B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of RMP version 8.1 to update the milestone for PASS study D6560R00004 regarding Arrythmia final report from 1H 2023 to 2H 2023

Action: For adoption of PRAC Assessment Report

5.2.2. Aclidinium, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP) - EMEA/H/C/003969/WS2546/0039; DUAKLIR GENUAIR (CAP) - EMEA/H/C/003745/WS2546/0040

Applicant: Covis Pharma Europe B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of RMP version 5.1 to update the milestone for PASS study D6560R00004 regarding Arrythmia final report from 1H 2023 to 2H 2023

Action: For adoption of PRAC Assessment Report

5.2.3. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0043

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of an updated RMP version 22.1 in order to remove existing additional pharmacovigilance activities (category 3 studies): Study I4V-MC-JAJA (JAJA) and Study I4V-MC-JAJD (JAJD)

Action: For adoption of PRAC Assessment Report

5.2.4. Emtricitabine, tenofovir disoproxil - EMTRICITABINE/TENOFOVIR DISOPROXIL ZENTIVA (CAP) - EMEA/H/C/004137/WS2486/0025

Applicant: Zentiva k.s.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP version 5.1 for Emtricitabine/Tenofovir disoproxil in line with the reference medicinal product Truvada (EMEA/H/C/WS2320)

Action: For adoption of PRAC Assessment Report

5.2.5. Ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/WS2537/0021; Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/WS2537/0020; Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - EMEA/H/C/004313/WS2537/0024

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP version 2.2 to update the final study report date for Study 8835-062 from 31 December 2023 to 31 October 2024, following approval of the post-authorisation measure procedure EMEA/H/C/004313-5/MEA/002.5

Action: For adoption of PRAC Assessment Report

5.2.6. 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

5.2.7. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS2535/0053; NEPARVIS (CAP) - EMEA/H/C/004343/WS2535/0051

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of a consolidated RMP for Entresto and its duplicate marketing

authorisation Neparvis following approval of: RMP version 4.2 (EMEA/H/C/004062/X/0044/G for Entresto and EMEA/H/C/004343/X/0042/G for Neparvis); RMP version 5.0 (EMEA/H/C/004062/WS2434/G for Entresto and EMEA/H/C/004343/WS2434/G for Neparvis) and RMP version 6.0 (EMEA/H/C/004062/WS2465 for Entresto and EMEA/H/C/004343/WS2465 for Neparvis)

Action: For adoption of PRAC Assessment Report

5.2.8. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/WS2541/0040; RYBELSUS (CAP) - EMEA/H/C/004953/WS2541/0035

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Submission of an updated RMP version 8.1 following assessment of the same for the reference product Wegovy (EMEA/H/C/005422/II/0009 approved on 28 April 2023). The Semaglutide RMP which is shared with all three Semaglutide products (Rybelsus, Ozempic, Wegovy) was updated due to an extension of the Wegovy label to include an indication in the adolescent population. The RMP's for for Rybelsus (oral semaglutide for treatment of Type 2 Diabetes) and Ozempic (subcutaneous semaglutide for treatment for Type 2 Diabetes) have been updated accordingly. Please note that no labelling changes will be made in this procedure because the investigation into efficacy and safety in paediatric population above 10 years of age according to agreed PIPs for Ozempic and Rybelsus is still ongoing

Action: For adoption of PRAC Assessment Report

5.2.9. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0064

Applicant: Amgen Europe B.V., ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of an updated RMP version 11.0 in order to remove the important potential risk of 'talimogene laherparepvec-mediated anti-GM-CSF antibody response', based on the accumulated scientific and clinical data

Action: For adoption of PRAC Assessment Report

5.2.10. Tecovirimat - TECOVIRIMAT SIGA (CAP) - EMEA/H/C/005248/II/0006

Applicant: SIGA Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of substantial updates to the protocol of study SIGA-246-021 listed as a specific obligation in the Annex II of the product information in order to reflect the transfer of sponsorship from SIGA Technologies, Inc. to the NIH Division of Microbiology and Infection Disease protocol. This is a phase 4, observational field study to evaluate safety and clinical benefit in tecovirimat-treated patients following exposure to variola virus and clinical diagnosis of smallpox disease. The Annex II and the RMP submitted version 1.2 are updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.11. Tixagevimab, cilgavimab - EVUSHELD (CAP) - EMEA/H/C/005788/II/0013

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of an updated RMP version 5 succession 1 to remove the commitment to conduct the PASS D8850R00006: A post-authorisation Observational Study of Women exposed to EVUSHELD During Pregnancy (O-STEREO)

Action: For adoption of PRAC Assessment Report

5.2.12. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0054

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP version 31.1 in order to modify study A3921427 from an interventional to a non-interventional study. In addition, the MAH has taken the opportunity to update other sections of the RMP

Action: For adoption of PRAC Assessment Report

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

5.3.1. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/II/0010

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include treatment of adolescents 12 to < 18 years of age with moderate to severe atopic dermatitis for CIBINQO based on final results from non-clinical study 00655292 [21GR211] and interim results from clinical study B7451015; this is a Phase III multi-center, long-term extension study investigating the efficacy and safety of abrocitinib, with or without topical medications, administered to subjects aged 12 years and older with moderate to severe atopic dermatitis. 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 4.1 of the RMP has also been submitted

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

5.3.2. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/II/0069, Orphan

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information following results from study PTC124-GD-041-DMD, listed as a specific obligation in the Annex II; this is a Phase 3 multicentre, randomised, double-blind, 18-month,

placebo-controlled study, followed by a 18-month open label extension to confirm the efficacy and safety of ataluren in the treatment of ambulant patients with nonsense mutation Duchenne muscular dystrophy (mnDMD) aged 5 years or older. Annex II, and Annex IIB are updated to delete the SOB and to reflect the switch from conditional to full marketing authorisation. The package leaflet is updated accordingly. The RMP version 11.0 has also been submitted. Minor corrections were done to align the product information with the latest QRD templates

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

5.3.3. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0078

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of section 5.1 of the SmPC in order to include the final overall survival (OS) analysis results based on final results from study WO30070 listed as a PAES in the Annex II to fulfil ANX/PAE 003; this is a Phase III, multicenter, randomised, placebo-controlled study of atezolizumab as monotherapy and in combination with platinum-based chemotherapy in patients with untreated locally advanced or metastatic urothelial carcinoma. The RMP version 27 has also been submitted. In addition, the MAH took the opportunity to update Annex II of the SmPC

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

5.3.4. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/II/0023, Orphan

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of adult patients with indolent systemic mastocytosis (ISM) for avapritinib based on results from the pivotal part of study BLU-285-2203 (PIONEER); this is a 3-part, randomised, double-blind, placebo-controlled, Phase 2 study to evaluate safety and efficacy of avapritinib (BLU-285) in indolent and smoldering systemic mastocytosis with symptoms inadequately controlled with standard therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 4.9, 5.1, 5.2 and 5.3 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

5.3.5. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0037

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include the treatment of paediatric patients (from 2 years of age and older) with moderate to severe atopic dermatitis for OLUMIANT, based on the final results from study I4V-MC-JAIP; this is a Phase III, multicentre, randomised, double blind, placebo controlled, parallel-group, outpatient study evaluating the pharmacokinetics, efficacy, and safety of baricitinib in paediatric patients with moderate-to-severe atopic

dermatitis. As a consequence sections 4.1, 4.2, 4.4, 4.5, 4.8, 4.9, 5.1, 5.2 of the SmPC are updated. The package leaflet has been updated accordingly. Version 17.1 of the RMP has also been submitted

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

5.3.6. 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. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/II/0021, Orphan

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: Extension of indication to include treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least 1 prior therapy, including an IMiD and a product information, have demonstrated disease progression on or after the last therapy and are refractory to lenalidomide for CARVYKTI, based on interim results from study MMY3002 listed as a specific obligation (SOB/006) in the Annex II. This is an ongoing, Phase 3, randomised, open-label, multicentre study to determine whether treatment with cilta-cel provides an efficacy benefit compared to standard therapy in participants with relapsed and lenalidomide-refractory multiple myeloma. As a consequence, sections 4.1, 4.4, 4.5, 4.8, 5.1 and 5.2 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 update Annex II of the product information. As part of the application the MAH is requesting a 1-year extension of the market protection

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

5.3.8. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/II/0027

Applicant: Merck Europe B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.5 and 4.6 of the SmPC in order to add information regarding the use of mavenclad with oral contraceptives based on the final study results from the drug-drug interaction study (MS 700568-0031). This is a randomised, double-blind, 2-period, 2-sequence, crossover Phase I study with a 1-month run-in period to examine the

effect of cladribine tablets on the pharmacokinetics of a monophasic oral contraceptive containing ethinyl estradiol and levonorgestrel (microgynon) in pre-menopausal women with Relapsing Multiple Sclerosis (RMS). The Annex II and package leaflet are updated accordingly. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity implement editorial changes to sections 4.2 and 4.4 of the SmPC

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

5.3.9. Entrectinib - ROZLYTREK (CAP) - EMEA/H/C/004936/X/0017/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Grouped application consisting of: 1) Extension application to: a) Introduce a new pharmaceutical form (coated granules) associated with a new strength (50 mg); b) Introduce a new route of administration (gastroenteral use) for the already authorised 100 mg and 200 mg hard capsules presentations based on final results from studies CO40778 (STARTRK-NG), GO40782 (STARTRK-2) and BO41932 (TAPISTRY). Study CO40778 is a Phase I/II open-label, dose-escalation and expansion study of entrectinib in pediatrics with locally advanced or metastatic solid or primary CNS tumors and/or who have no satisfactory treatment options; Study GO40782 is an open-label, multicenter, global Phase II basket study of entrectinib for the treatment of patients with solid tumors that harbor an NTRK1/2/3, ROS1, or ALK gene rearrangement (fusion), and Study BO41932 is a Phase II, global, multicenter, open-label, multi-cohort study designed to evaluate the safety and efficacy of targeted therapies or immunotherapy as single agents or in rational, specified combinations in participants with unresectable, locally advanced or metastatic solid tumors determined to harbor specific oncogenic genomic alterations or who are tumor mutational burden (TMB)-high as identified by a validated next-generation sequencing (NGS) assay, grouped with the following type II variations:

a) to extend the currently approved indication in solid tumours with NTRK gene fusion to patients from birth to 12 years of age (both for the coated granules and already approved hard capsules presentations);

b) to add a new paediatric indication from birth to 18 years of age for patients with solid tumours with a ROS1 gene fusion (both for the coated granules and already approved hard capsules presentations).
As a consequence, sections 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 accordingly. The package leaflet and Labelling are updated in accordance.

c) to add wording regarding the option of suspension in water of the content of the capsules to be used orally or via the e.g. gastric or nasogastric tube (in sections 4.2 and 5.2 of the SmPC).

The RMP (version 5) is updated in accordance. The MAH took the opportunity to introduce minor editorial changes to the product information and to update Annex II of the SmPC

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

5.3.10. Evinacumab - EVKEEZA (CAP) - EMEA/H/C/005449/II/0011

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include the treatment of paediatric patients with homozygous familial hypercholesterolaemia (HoFH) aged 5 years and older for EVKEEZA, based on interim results from study R1500-CL-17100, as well as supportive information from an updated interim analysis of study R1500-CL-1719, and an extrapolation analysis (including population PK, population PK/PD, and simulation analyses). R1500-CL-17100 is an ongoing multicentre, three-part, single-arm, open-label study evaluating the efficacy, safety, and tolerability of evinacumab in paediatric patients aged ≥ 5 to 11 years with HoFH. 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 1.1 of the RMP has also been submitted. In addition, the marketing authorisation holder took the opportunity to introduce minor editorial changes to the product information. Furthermore, the product information is brought 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

5.3.11. Fexinidazole - FEXINIDAZOLE WINTHROP (Art 58[4]) - EMEA/H/W/002320/II/0016

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of indication to include treatment of both first stage (haemo-lymphatic) and second stage (meningo-encephalitic) of human African trypanosomiasis (HAT) due to Trypanosoma brucei rhodesiense for FEXINIDAZOLE WINTHROP based final results from study DNDI-FEX-07-HAT - Efficacy and safety of fexinidazole in patients with Human African Trypanosomiasis (HAT) due to Trypanosoma brucei rhodesiense: a multicentre, open-label clinical trial; this is a phase-II/III, multicenter, open-label, non-randomised, single-arm clinical trial to assess the efficacy and safety of fexinidazole in patients with r-HAT. As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted

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

5.3.12. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0013/G, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final reports from studies ALN-AS1-003 (Study 003) and ALN-AS1-002 (Study 002) listed as a category 3 studies in the RMP. Study 003 is a phase 3 randomised, double-blind, placebo-controlled multicenter study with an open-label extension to evaluate the efficacy and safety of givosiran in patients with acute hepatic porphyrias, while Study 002 is a multicentre, open-label extension study to evaluate the long-term safety and clinical activity of subcutaneously administered ALN AS1 in patients with acute intermittent porphyria who have completed a previous clinical study with ALN-AS1. The RMP version 2.2 has also been submitted

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

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

5.3.13. Human fibrinogen, human thrombin - VERASEAL (CAP) - EMEA/H/C/004446/II/0027

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of children for VeraSeal, based on final results from study IG1405; this is a prospective, randomised, active-controlled, single-blind, parallel group clinical trial to evaluate the safety and efficacy of VeraSeal as an adjunct to haemostasis during surgery in paediatric subjects. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 6.0 of the RMP has also been submitted

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

5.3.14. Human normal immunoglobulin - HYQVIA (CAP) - EMEA/H/C/002491/II/0087

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) in adults for HyQvia, based on final results from studies 161403 and ABV-771-1001; and interim results from study 161505. 161403 and 161505 are interventional Phase III efficacy and safety studies respectively, while ABV-771-1001 is an interventional Phase I safety study. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and labelling are updated in accordance. Version 14.0 of the RMP has also been submitted

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

5.3.15. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/II/0133

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Submission of the final report from study CSTI571I2201 - A European observational registry collecting efficacy and safety data in newly diagnosed paediatric Ph+ acute lymphocytic leukaemia (ALL) patients treated with chemotherapy plus imatinib and with or without haematopoietic stem cell transplantation (HSCT), listed as an obligation in the Annex II of the product information. This study has been designed as an observational, multi-centre registry to collect efficacy and safety data in Ph+ ALL paediatric patients (ages 1 to <18 years old) treated with chemotherapy plus imatinib, with or without HSCT, primarily in European countries. The Annex II and the RMP (version 13.0) are updated accordingly

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

5.3.16. Inotuzumab ozogamicin - BESPONSA (CAP) - EMEA/H/C/004119/II/0026, Orphan

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.2, 4.6, 4.8, 5.1 and 5.2 of the SmPC in order to update paediatric information based on final results from studies ITCC-059 (WI203581) and INO-Ped-ALL-1 (WI235086). Study WI203581 is a Phase 1/2, multicenter, European, multi-cohort, open-label study in pediatric patients (⩾1 and <18 years of age) with R/R CD22-positive Acute Lymphoblastic Leukemia (ALL); and study WI235086 is an open-label, multi-center Phase 1 study to assess safety and tolerability of InO in Japanese pediatric patients with R/R CD22-positive ALL. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted

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

5.3.17. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0035, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.8 and 5.1 of the SmPC based on interim results from study VX19-445-107 (Study 107) listed as a category 3 study in the RMP; this is a Phase III, open-label study evaluating the long-term safety and efficacy of VX445/TEZ/IVA combination therapy in subjects with cystic fibrosis who 6 years of age and older. The RMP version 7.0 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

5.3.18. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0039, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update information based on final results from study VX17-445-105 (study 105); this is a phase 3, open-label, extension study evaluating the long-term safety and efficacy of ELX/TEZ/IVA treatment in cystic fibrosis (CF) subjects 12 years of age and older, homozygous, or heterozygous for the F508del-CFTR mutation who participated in study VX17-445-102 (study 102) or study VX17-445-103 (study 103). The RMP version 7.2 has also been submitted

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

5.3.19. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/X/0033, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Extension application to add a new pharmaceutical form (granules) associated with 2 new strengths (60 mg/40 mg/80 mg and 75 mg/50 mg/100 mg) to support a new indication in a combination regimen with ivacaftor for the treatment of cystic fibrosis (CF) in paediatric patients aged 2 to less than 6 years who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene (see section 5.1). The new indication is only applicable to the new granules pharmaceutical form. As a consequence of the line extension the product information for the film coated tablets is also updated to reflect the addition of a new pharmaceutical form. The RMP (version 6.2) has also been submitted

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

5.3.20. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0045, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the Clinical Study Report (Addendum 2) for study C16019 listed as a Specific Obligation in the Annex II of the product information. This is a phase 3, randomised, double-blind, placebo-controlled study of single-agent oral ixazomib as maintenance therapy following autologous stem cell transplant (ASCT) for patients with newly diagnosed multiple myeloma. In addition, the MAH proposes to remove NINLARO from the list of medicines subject to additional monitoring and to remove the black triangle from the SmPC. The Annex II and package leaflet are updated accordingly. The RMP version 10.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information and 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

5.3.21. Lanadelumab - TAKHZYRO (CAP) - EMEA/H/C/004806/X/0034/G, Orphan

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped application consisting of: 1) Extension application to add a new strength of 150 mg for lanadelumab solution for injection in pre-filled syringe and to extend the indication to include paediatric use (2 to <12 years). The new indication is only applicable to the new 150 mg strength presentations. The RMP (version 3.0) is updated in accordance; 2) a type IB variation (C.I.z) to update section 7 of the package leaflet (PL) for the 300 mg in 2 ml pre-filled syringe (EU/1/18/1340/004-006) in line with the proposed package leaflet for the 150 mg in 1 ml pre-filled syringe (new strength). In addition, the MAH has requested an extension of the Orphan Market Exclusivity from 10 to 12 years

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

5.3.22. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/II/0050

Applicant: Eisai GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update paediatric information based on final results from studies E7080-G000-207 and E7080-G000-230. Study E7080-G000-207 is a multicenter, open-label, Phase 1/2 study of lenvatinib in children and adolescents with refractory or relapsed solid malignancies and young adults with osteosarcoma; Study E7080-G000-230 is a multicenter, open-label, randomised Phase 2 study to compare the efficacy and safety of lenvatinib in combination with ifosfamide and etoposide versus ifosfamide and etoposide in children, adolescents and young adults with Relapsed or Refractory Osteosarcoma (OLIE). The package leaflet is updated accordingly. The RMP version 15.1 has also been submitted

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

5.3.23. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/II/0080

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.2, 4.6, and 4.8 of the SmPC in order to modify administration instructions recommendation regarding the monitoring of pre-prandial blood glucose in pre prandial condition and in case of symptoms and to prevent the risk of lipohypertrophy, delete wording in the pregnancy section and update on number of patients with severe primary IGD deficiency (IGFD) based on the cumulative review of safety database, scientific literature and clinical trials data. The package leaflet is updated accordingly. The RMP version 14.0 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

5.3.24. Methotrexate - NORDIMET (CAP) - EMEA/H/C/003983/II/0027

Applicant: Nordic Group B.V.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of moderate to severe recalcitrant disabling psoriasis for Nordimet, based on literature. As a consequence, sections 4.1 and 4.2 of the SmPC are updated. The package leaflet is updated in accordance. The RMP (version 6.0) of the RMP has also been submitted

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

5.3.25. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/X/0132

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

Scope: Extension application to introduce a new recombinant Chinese hamster ovary (CHO) host monoclonal cell line (BMSCHO1-nivolumab) and a new manufacturing process of the active substance . The RMP (version 34) is updated in accordance. In addition, the MAH took the opportunity to update the Annex II in the product information. Consequentially, the following manufacturers of the biological active substance have been removed from the dossier (module 3.2.S.2.1 and Annex II of the product information):

- Lotte Biologics USA, LLC (6000 Thompson Road, East Syracuse, New York 13057, USA)
- Lonza Biologics, Inc. (101 International Drive, Portsmouth, New Hampshire 03801, USA)
- Samsung Biologics Co. Ltd. (300, Songdo Bio Way (Daero), Yeonsu-gu, Incheon, 21987, Korea)

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

5.3.26. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0064

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.8 and 5.1 of the SmPC to update the results of a descriptive analysis of Overall Survival at seven years last subject randomised in study D0818C0001 (SOLO1). This is a Phase III randomised, double blind, placebo controlled, multicentre study in which advanced ovarian cancer patients with BRCA mutations who had responded following first-line platinum-based chemotherapy were randomised 2:1 to receive either Olaparib (300 mg bd, tablet formulation) or placebo. The RMP version 28 has also been submitted. In addition, the MAH took the opportunity to update section D of Annex II

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

5.3.27. Onasemnogene abeparvovec - ZOLGENSMA (CAP) - EMEA/H/C/004750/II/0040, Orphan

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to add a new warning and precaution capturing the theoretical risk of tumorigenicity as a result of vector integration and to include a new statement indicating random instances of vector integration are possible; based on final results from studies 2220205 and 2220117, and literature. The package leaflet is updated accordingly. The RMP version 3 has also been submitted

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

5.3.28. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0052

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 5.1 of the SmPC in order to update efficacy information (final OS data) based on final results from study D5164C00001 (ADAURA) listed as a PAES in the Annex II; this is a Phase III, double-blind, randomised, placebo-controlled study, designed to assess the efficacy and safety of osimertinib versus placebo in patients with stage IB-IIIA epidermal growth factor receptor mutation positive (EGFRm) non-small cell lung cancer (NSCLC) who have undergone complete tumour resection, with or without postoperative adjuvant chemotherapy. The RMP version 15 has also been submitted. In addition, the MAH took the opportunity to update Annex II section D of the product information and to implement editorial changes to the SmPC

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

5.3.29. Patiromer - VELTASSA (CAP) - EMEA/H/C/004180/X/0031/G

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kirsti Villikka

Scope: Extension application to introduce a new strength (1 g powder for oral suspension), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of population from 6 to 18 years old for Veltassa based on final results from paediatric study RLY5016-206P (EMERALD); this is a phase 2, open-label, multiple dose study to evaluate the pharmacodynamic effects, safety, and tolerability of patiromer for oral suspension in children and adolescents 2 to less than 18 years of age with chronic kidney disease and hyperkalaemia. As a consequence, sections 1, 2, 4.1, 4.2, 4.8, 4.9, 5.1 and 6.5 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. Version 2 of the RMP 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

5.3.30. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0121

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include Keytruda as monotherapy for the adjuvant treatment of adults with stage IB (T2a $\geqslant$ 4 cm), II or IIIA non-small cell lung carcinoma (NSCLC) who have undergone complete resection, based on study KEYNOTE-091: an ongoing phase 3, randomised, triple-blinded, placebo-controlled, multicentre study of pembrolizumab versus placebo in patients with early-stage NSCLC after resection and completion of standard adjuvant therapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are being updated and the package leaflet is updated in accordance. An updated RMP version 39.1 was also submitted

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

5.3.31. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0138

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include KEYTRUDA in combination with gemcitabine-based chemotherapy for the first-line treatment of locally advanced unresectable or metastatic biliary tract carcinoma in adults, based on final results from study KEYNOTE-966; this is a Phase 3 randomised, double-blind study of Pembrolizumab plus Gemcitabine/Cisplatin versus Placebo plus Gemcitabine/Cisplatin as first-line therapy in participants with advanced and/or unresectable biliary tract carcinoma. As a consequence, sections 4.1, 4.4 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 43.1 of the RMP has also been submitted

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

5.3.32. 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

5.3.33. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/II/0036

Applicant: Zr Pharma& GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include maintenance treatment of adult patients with advanced (FIGO Stages III and IV) epithelial ovarian (EOC), fallopian tube (FTC), or primary peritoneal cancer (PPC) who are in response (complete or partial) to first-line platinum-based chemotherapy for RUBRACA, based on interim results from study CO-338-087 (ATHENA); this is a Phase III, randomised, double-blind, dual placebo controlled study of rucaparib as monotherapy and in combination with nivolumab in patients with newly diagnosed EOC, FTC, or PPC who have responded to their first-line treatment (surgery and platinum-based chemotherapy). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 6.3 of the RMP has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection

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

5.3.34. Tepotinib - TEPMETKO (CAP) - EMEA/H/C/005524/II/0009

Applicant: Merck Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy information based on results from study VISION (MS200095-0022); this is a Phase II, multicenter, open-label, single-arm study to evaluate the efficacy and safety/tolerability of the recommended dose of tepotinib in participants with advanced NSCLC of all histology types who tested positive for METex14 skipping alterations by next-generation sequencing in tissue (RNA-based) or plasma (circulating tumor DNA based). The RMP version 2.0 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

5.3.35. Vosoritide - VOXZOGO (CAP) - EMEA/H/C/005475/II/0006, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: Extension of indication to include treatment of children less than 2 years of age for Voxzogo, based on the final results from the category 1 study BMN 111-206 and interim results from its open-label extension study 111-208. 111-206 is a phase 2 randomised, double-blind, placebo-controlled, multicentre study to assess the safety and efficacy of BMN 111 in infants and young children with achondroplasia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Annex II and package leaflet are updated in accordance. Version 3.0 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

6. Periodic safety update reports (PSURs)

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

6.1.1. (1r,2s,5s)-n-{(1s)-1-cyano-2-[(3s)-2-oxopyrrolidin-3-yl]ethyl}-6,6-dimethyl-3- [3-methyl-n-(trifluoroacetyl)-l-valyl]-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir (Paxlovid) - PAXLOVID (CAP) - PSUSA/00010984/202212

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Abatacept - ORENCIA (CAP) - PSUSA/00000013/202212

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Adalimumab - AMGEVITA (CAP); AMSPARITY (CAP); HEFIYA (CAP); HUKYNDRA (CAP); HULIO (CAP); HUMIRA (CAP); HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP); LIBMYRIS (CAP); YUFLYMA (CAP) - PSUSA/00010783/202212

Applicant: Amgen Europe B.V. (AMGEVITA), Pfizer Europe MA EEIG (Amsparity), STADA Arzneimittel AG (Hukyndra, Libmyris), Viatris Limited (Hulio), AbbVie Deutschland GmbH & Co. KG (Humira), Sandoz GmbH (Hefiya, Hyrimoz), Fresenius Kabi Deutschland GmbH (Idacio), Samsung Bioepis NL B.V. (Imraldi), Celltrion Healthcare Hungary Kft. (Yuflyma)

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Anifrolumab - SAPHNELO (CAP) - PSUSA/00010980/202301

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Ataluren - TRANSLARNA (CAP) - PSUSA/00010274/202301

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Avalglucosidase alfa - NEXVIADYME (CAP) - PSUSA/00011002/202302

Applicant: Sanofi B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Avapritinib - AYVAKYT (CAP) - PSUSA/00010878/202301

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Belantamab mafodotin - BLENREP (CAP) - PSUSA/00010869/202302

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Birch bark extract[5] - FILSUVEZ (CAP) - PSUSA/00010446/202301

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Botulinum toxin type A[6] - NUCEIVA (CAP) - PSUSA/00010796/202301

Applicant: Evolus Pharma B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Brexucabtagene autoleucel - TECARTUS (CAP) - PSUSA/00010903/202301

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.12. Bulevirtide - HEPCLUDEX (CAP) - PSUSA/00010873/202301

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Casirivimab, imdevimab (Ronapreve) - RONAPREVE (CAP) - PSUSA/00010963/202301

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[5] Centrally authorised product(s) only
[6] Centrally authorised product(s) only

6.1.14. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - PSUSA/00010028/202212

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[7]) - EMEA/H/W/002168/PSUV/0021

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser; PRAC Co-rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.16. Daridorexant - QUVIVIQ (CAP) - PSUSA/00010993/202301

Applicant: Idorsia Pharmaceuticals Deutschland GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Darolutamide - NUBEQA (CAP) - PSUSA/00010843/202301

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dasabuvir - EXVIERA (CAP); ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - PSUSA/00010773/202301

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.1.19. Defatted powder of Arachis hypogaea L., semen (peanuts) - PALFORZIA (CAP) - PSUSA/00010902/202301

Applicant: Aimmune Therapeutics Ireland Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Dolutegravir - TIVICAY (CAP); dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP); dolutegravir, lamivudine - DOVATO (CAP) - PSUSA/00010075/202301

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Eptacog beta (activated) - CEVENFACTA (CAP) - PSUSA/00011006/202301

Applicant: Laboratoire Francais du Fractionnement et des Biotechnologies

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Eptifibatide - INTEGRILIN (CAP) - PSUSA/00001246/202301

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Faricimab - VABYSMO (CAP) - PSUSA/00011016/202301

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Finerenone - KERENDIA (CAP) - PSUSA/00010978/202301

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Fostemsavir - RUKOBIA (CAP) - PSUSA/00010911/202302

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Glucagon[8] - BAQSIMI (CAP); OGLUO (CAP) - PSUSA/00010826/202301

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

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Glucarpidase - VORAXAZE (CAP) - PSUSA/00010968/202301

Applicant: SERB S.A.S.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Ibritumomab tiuxetan - ZEVALIN (CAP) - PSUSA/00001704/202302

Applicant: Ceft Biopharma s.r.o.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.29. Imipenem, cilastatin, relebactam - RECARBRIO (CAP) - PSUSA/00010830/202301

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[8] Centrally authorised product(s) only

6.1.30. Inclisiran - LEQVIO (CAP) - PSUSA/00010904/202212

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Lisocabtagene maraleucel, lisocabtagene maraleucel - BREYANZI (CAP) - PSUSA/00010990/202302

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.32. Lixisenatide - LYXUMIA (CAP) - PSUSA/00010017/202301

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Lonoctocog alfa - AFSTYLA (CAP) - PSUSA/00010559/202301

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Melphalan flufenamide - PEPAXTI (CAP) - PSUSA/00011013/202302

Applicant: Oncopeptides AB

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Metreleptin - MYALEPTA (CAP) - PSUSA/00010700/202301

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Odevixibat - BYLVAY (CAP) - PSUSA/00010949/202301

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Omalizumab - XOLAIR (CAP) - PSUSA/00002214/202212

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Osilodrostat - ISTURISA (CAP) - PSUSA/00010820/202301

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Plerixafor - MOZOBIL (CAP) - PSUSA/00002451/202212

Applicant: Sanofi B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Pneumococcal polysaccharide conjugate vaccine (15 valent, adsorbed) - VAXNEUVANCE (CAP) - PSUSA/00010975/202301

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Pneumococcal polysaccharide conjugate vaccine (10-valent, adsorbed) - SYNFLORIX (CAP) - PSUSA/00009262/202212

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - PREVENAR 13 (CAP) - PSUSA/00009263/202301 (with RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Quadrivalent influenza vaccine (recombinant, prepared in cell culture) - SUPEMTEK (CAP) - PSUSA/00010886/202301

Applicant: Sanofi Pasteur

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Ravulizumab - ULTOMIRIS (CAP) - PSUSA/00010787/202212

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Regdanvimab - REGKIRONA (CAP) - PSUSA/00010964/202302

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Valentina Di Giovanni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Relugolix - ORGOVYX (CAP) - PSUSA/00010994/202301

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Remimazolam - BYFAVO (CAP) - PSUSA/00010924/202301

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Risdiplam - EVRYSDI (CAP) - PSUSA/00010925/202302

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Romosozumab - EVENITY (CAP) - PSUSA/00010824/202301

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Rufinamide - INOVELON (CAP) - PSUSA/00002671/202301

Applicant: Eisai GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Salmeterol, fluticasone propionate[9] - BROPAIR SPIROMAX (CAP); SEFFALAIR SPIROMAX (CAP) - PSUSA/00010928/202301

Applicant: Teva B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Sarilumab - KEVZARA (CAP) - PSUSA/00010609/202301

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Monica Martinez Redondo

[9] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Smallpox vaccine and monkeypox (live, modified vaccinia virus Ankara) - IMVANEX (CAP) - PSUSA/00010119/202301

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Sutimlimab - ENJAYMO (CAP) - PSUSA/00011023/202302

Applicant: Sanofi B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Tafasitamab - MINJUVI (CAP) - PSUSA/00010951/202301

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Tecovirimat - TECOVIRIMAT SIGA (CAP) - PSUSA/00010971/202301

Applicant: SIGA Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.57. Tipranavir - APTIVUS (CAP) - PSUSA/00002973/202212 (with RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. Ustekinumab - STELARA (CAP) - PSUSA/00003085/202212

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.59. Vericiguat - VERQUVO (CAP) - PSUSA/00010950/202301

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.60. Voclosporin - LUPKYNIS (CAP) - PSUSA/00011020/202301

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.61. Vonicog alfa - VEYVONDI (CAP) - PSUSA/00010714/202212

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Mari Thorn

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. ^{13}C-urea, ^{14}C-urea - HELICOBACTER TEST INFAI (CAP); PYLOBACTELL (CAP); NAP - PSUSA/00000006/202301

Applicant: INFAI GmbH (Helicobacter Test INFAI), Richen Europe S.r.l. (Pylobactell), various

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Abacavir - ZIAGEN (CAP); NAP - PSUSA/00000010/202212

Applicant: ViiV Healthcare B.V. (Ziagen), various

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Abacavir, lamivudine - KIVEXA (CAP); NAP - PSUSA/00000011/202212

Applicant: ViiV Healthcare B.V. (Kivexa), various

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Abacavir, lamivudine, zidovudine - TRIZIVIR (CAP); NAP - PSUSA/00003144/202212

Applicant: ViiV Healthcare B.V. (Trizivir), various

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Lenalidomide - LENALIDOMIDE ACCORD (CAP); LENALIDOMIDE KRKA (CAP); LENALIDOMIDE KRKA D.D. (SRD) (CAP); LENALIDOMIDE KRKA D.D. NOVO MESTO (CAP); LENALIDOMIDE MYLAN (CAP); REVLIMID (CAP); NAP - PSUSA/00001838/202212

Applicant: Accord Healthcare S.L.U. (Lenalidomide Accord), Krka d.d. Novo mesto (Lenalidomide Krka), KRKA, d.d., Novo mesto (Lenalidomide Krka d.d. (SRD), Lenalidomide Krka d.d. Novo mesto), Mylan Ireland Limited (Lenalidomide Mylan), Bristol-Myers Squibb Pharma EEIG (Revlimid), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Oxybutynin - KENTERA (CAP); NAP - PSUSA/00002253/202207

Applicant(s): Teva B.V. (Kentera), various

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of a revised PRAC Recommendation (via written procedure adopted on 01 August 2023) to CHMP

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

6.3.1. 5-fluorouracil[10] (NAP) - PSUSA/00010000/202301

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Allergen for therapy: Dactylis Glomerata L., Phleum Pratense L., Anthoxanthum Odoratum L., Lolium Perenne L., Poa Pratensis L.[11] (NAP) - PSUSA/00010465/202212

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Acebutolol (NAP) - PSUSA/00000018/202212

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Aldesleukin (NAP) - PSUSA/00000076/202212

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Alitretinoin[12] (NAP) - PSUSA/00010710/202301

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

[10] For topical formulation(s) only
[11] Sublingual tablet only
[12] Oral use only

Action: For adoption of recommendation to CMDh

6.3.6. Amisulpride (NAP) - PSUSA/00000167/202301

Applicant(s): various

PRAC Lead: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Atracurium (NAP) - PSUSA/00000267/202212

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Calcium chloride dihydrate, magnesium chloride hexahydrate, malic acid, sodium acetate trihydrate, sodium chloride, potassium chloride/calcium chloride dihydrate, sodium chloride, sodium lactate, potassium chloride/calcium chloride, sodium chloride, potassium chloride (NAP) - PSUSA/00010622/202301

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Cefprozil (NAP) - PSUSA/00000605/202212

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Cilostazol (NAP) - PSUSA/00010209/202301

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Cimicifuga racemosa (L.) Nutt., rhizoma (NAP) - PSUSA/00000755/202301

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Cisplatin (NAP) - PSUSA/00000778/202212

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Codeine camphosulphonate, sodium benzoate, codeine camphosulphonate, sulfogaiacol, grindelia soft extract (NAP) - PSUSA/00010542/202212

Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Enalapril, nitrendipine (NAP) - PSUSA/00001213/202301

Applicant(s): various

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Felodipine (NAP) - PSUSA/00001356/202212

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Furosemide (NAP) - PSUSA/00001491/202301

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Gemcitabine (NAP) - PSUSA/00001519/202301

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Haemophilus influenzae, klebsiella ozaenae, klebsiella pneumoniae, moraxella catarrhalis, staphylococcus aureus, streptococcus pneumoniae, streptococcus pyogenes, streptococcus viridans vaccine (NAP) - PSUSA/00001582/202212

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Hypericum perforatum L., herba (NAP) - PSUSA/00001701/202301

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Ibutilide (NAP) - PSUSA/00001713/202212

Applicant(s): various

PRAC Lead: Georgia Gkegka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Levobupivacaine (NAP) - PSUSA/00001848/202212

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Paroxetine (NAP) - PSUSA/00002319/202212

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Sertindole (NAP) - PSUSA/00002695/202301

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Tetanus vaccines (NAP) - PSUSA/00002910/202301

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/LEG 015.3

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 015.2 [Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) adopted in September 2021] as per the request for supplementary information (RSI) adopted in February 2023

Action: For adoption of advice to CHMP

6.4.2. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/LEG 010.3

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 010.2 [Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) adopted in September 2021] as per the

request for supplementary information (RSI) adopted in February 2023

Action: For adoption of advice to CHMP

6.4.3. Dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/LEG 005.3

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: David Olsen

Scope: MAH's response to LEG 005.2 [Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) adopted in September 2021] as per the request for supplementary information (RSI) adopted in February 2023

Action: For adoption of advice to CHMP

6.4.4. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/LEG 021

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of further data on cases of secondary malignancies, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010702/202208) adopted in March 2023

Action: For adoption of advice to CAT and CHMP

6.4.5. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/LEG 063

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of cumulative reviews of cases of psychiatric disorders including depression and related disorders, ulcerative keratitis, and pyoderma gangrenosum from clinical trials data, post-marketing studies, literature and spontaneous reports as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002980/202204) adopted in December 2022

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0063

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of an update of sections 4.3, 4.4 and 4.5 of the SmPC to update and

streamline the relevant wording on opioids as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010366/202209) adopted in April 2023. The package leaflet is updated accordingly. The RMP version 12.9 has also been submitted

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[13]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[14]

7.1.1. Fosdenopterin – NULIBRY (CAP) - EMEA/H/C/PSP/S/0103.1

Applicant: Zydus France S.A.S.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/0103 [PASS to characterise and assess the long-term safety and efficacy of NULIBRY prescribed in routine practice for patients with MoCD Type A] as per the request to supplementary information (RSI) adopted in April 2023

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[15]

7.2.1. Birch bark extract - FILSUVEZ (CAP) - EMEA/H/C/005035/MEA 001.1

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Zane Neikena

Scope: MAH’s response to MEA 001 [Submission of a protocol for Filsuvez Observational Safety and Effectiveness Evaluation Registry-based study in epidermolysis bullosa (EB) (FOStER-EB) [(AEB-21)] (listed as category 3 study in the RMP) to evaluate the long-term safety of Filsuvez amongst patients treated for EB in relation to the incidence, severity and relatedness of skin malignancies (including squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and malignant melanoma (MM)), and use in patients with different skin types regarding ethnic origin] as per request for supplementary information (RSI) adopted in March 2023

Action: For adoption of advice to CHMP

[13] 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
[14] In accordance with Article 107n of Directive 2001/83/EC
[15] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

7.2.2. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/MEA 002.7

Applicant: LEO Pharma A/S

PRAC Rapporteur: Monica Martinez Redondo

Scope: Revised protocol (version 6.0) for PASS KYNTHEUM-1345: The BRodalumab Assessment of Hazards: A Multinational Safety (BRAHMS) study in electronic healthcare databases – an observational PASS of suicidal behaviour, serious infections, major adverse cardiac events (MACE) and malignancy in psoriasis patients treated with brodalumab (Kyntheum)

Action: For adoption of advice to CHMP

7.2.3. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/MEA 007.2

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: MAH's response to MEA 007.1 [Submission of a revised protocol for study PCSONCA0014: a survey to evaluate the effectiveness of the ciltacabtagene autoleucel HCP Educational Program and the Product Handling Training] as per the request for supplementary information (RSI) adopted in April 2023

Action: For adoption of advice to CAT and CHMP

7.2.4. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 006.2

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Updated protocol version 3.0 for study 2019nCoV-404: US PASS to evaluate the pooled of risk of selected adverse events of special interest (AESI) within specified time periods after vaccination with Nuvaxovid using a claim and/or electronic healthcare record (her) database

Action: For adoption of advice to CHMP

7.2.5. Deucravacitinib - SOTYKTU (CAP) - EMEA/H/C/005755/MEA 001

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study IM011194: long-term, observational cohort study of adults with plaque psoriasis, who are new users of deucravacitinib, non-TNFi (tumor necrosis factor inhibitor) biologics, TNFi biologics, or non-biologic systemic therapy in the real-world clinical setting (IM011194) to evaluate the long-term safety of deucravacitinib in patients with psoriasis in the real-world setting

Action: For adoption of advice to CHMP

7.2.6. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/MEA 012

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Protocol for study BO44691: PASS to evaluate the long-term safety of Hemlibra in patients with moderate Hemophilia A and severe bledding phenotype (safety risk: thrombo-embolic events)

Action: For adoption of advice to CHMP

7.2.7. Fexinidazole - FEXINIDAZOLE WINTHROP (Art 58[16]) - EMEA/H/W/002320/MEA 002.3

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002.2 [Protocol for study FEXINC09395: a prospective observational study of the safety of fexinidazole for human African trypanosomiasis] as per the request for supplementary information (RSI) adopted in April 2023

Action: For adoption of advice to CHMP

7.2.8. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 016.3

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 016.2 [Revised protocol for study GLPG0634-CL-413: a non-interventional, PASS of filgotinib in patients with moderately to severely active ulcerative colitis (a European multi registry-based study) as per the request for supplementary information (RSI) adopted in March 2023

Action: For adoption of advice to CHMP

7.2.9. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 017

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GLPG0634-CL-417: non-interventional, post-authorisation, cohort, safety study evaluating the effectiveness of the additional risk minimization measures for filgotinib (Jyseleca) use in patients with moderately to severely active ulcerative colitis within multiple European registries

Action: For adoption of advice to CHMP

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

7.2.10. Maribavir - LIVTENCITY (CAP) - EMEA/H/C/005787/MEA 005

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Adam Przybylkowski

Scope: Protocol version 1.0 for study TAK-620-4007: Retrospective chart review of safety outcomes associated with use of maribavir in patients with post-transplant refractory cytomegalovirus (CMV) infection and comorbid endstage renal disease (ESRD) or comorbid severe chronic renal disease requiring peritoneal dialysis or hemodialysis

Action: For adoption of advice to CHMP

7.2.11. Niraparib, abiraterone acetate - AKEEGA (CAP) - EMEA/H/C/005932/MEA 001

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Feasibility assessment for a PASS to characterize the risk of second primary malignancies (SPM) including MDS/AML among metastatic prostate cancer patients exposed to AKEEGA

Action: For adoption of advice to CHMP

7.2.12. Nivolumab, relatlimab - OPDUALAG (CAP) - EMEA/H/C/005481/MEA 001

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

Scope: Protocol for study CA224122 to evaluate Grades 3-4 AEs (which includes irARs) experienced by paediatric patients ≥ 12 to < 18 years of age, along with their management, and outcome. Secondary objectives include evaluating long-term outcomes (with emphasis on growth and development)

Action: For adoption of advice to CHMP

7.2.13. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 003.5

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol amendment for study 165-501: a multicentre, prospective global observational study to evaluate the long term safety of subcutaneous injections of pegvaliase in patients with phenylketonuria

Action: For adoption of advice to CHMP

7.2.14. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 001.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Updated protocol and second annual interim report for study BHV3000-402: a Prospective, Registry-based, Observational Study to Assess Maternal, Fetal, and Infant Outcomes following Exposure to Rimegepant: The Migraine Observational Nurtec Pregnancy Registry (MONITOR)

Action: For adoption of advice to CHMP

7.2.15. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 002.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Updated protocol and second annual interim report for study BHV3000-402: a Prospective, Registry-based, Observational Study to Assess Maternal, Fetal, and Infant Outcomes following Exposure to Rimegepant: The Migraine Observational Nurtec Pregnancy Registry (MONITOR)

Action: For adoption of advice to CHMP

7.2.16. Solriamfetol - SUNOSI (CAP) - EMEA/H/C/004893/MEA 002.3

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Julia Pallos

Scope: Submission of a revised protocol (version no. 4.0) for study JZP865-401: a PASS to evaluate the long-term safety of solriamfetol in adult patients with obstructive sleep apnoea (OSA) treated with solriamfetol

Action: For adoption of advice to CHMP

7.2.17. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 018.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 018.2 and revised protocol for study A3921407: a post-authorisation active safety surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile PsA within the German Biologics in Pediatric Rheumatology Registry (BIKER) and within the Juvenile Arthritis Methotrexate/Biologics long-term Observation (JuMBO) Registry

Action: For adoption of advice to CHMP

7.2.18. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 019.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 019.2 and revised protocol for study 3921408: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the Swedish juvenile

idiopatic arthritis (JIA) clinical registry

Action: For adoption of advice to CHMP

7.2.19. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 020.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 020.2 and revised protocol for study A3921409: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the UK juvenile idiopathic arthritis (JIA) biologics register

Action: For adoption of advice to CHMP

7.2.20. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 025.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 025 and revised protocol for study No921403 [(listed as category 3 study in the RMP): a PASS of the Utilisation and Prescribing Patterns of Xeljanz (tofacitinib) Using an Administrative Healthcare Database in France: a descriptive drug utilisation study using real-world data collected from routine clinical care in France. The overall goal is to determine if there is evidence that prescribers in France are compliant with the recommendations and limitations for use described in the tofacitinib additional risk minimisation measures (aRMM) materials] as per the request for supplementary information (RSI) adopted in March 2023

Action: For adoption of advice to CHMP

7.2.21. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 017.7

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Protocol amendment for study C4591021 (previously known as vACcine Covid-19 monitoring readinESS/Vaccine monitoring Collaboration for Europe (ACCESS/VAC4EU)): an assessment of potential increased risk of adverse events of special interest (AESI), including myocarditis/pericarditis after being vaccinated with COVID-19 messenger ribonucleic acid (mRNA) vaccine estimating the time trend, in relation to DHPC letter dissemination, of the proportion of individuals who received real-world clinical assessments for myocarditis/pericarditis following Comirnaty (tozinameran) vaccination

Action: For adoption of advice to CHMP

7.2.22. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 062.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a protocol for study C4591052: a PASS of the Pfizer-BioNTech COVID-19 bivalent Omicron-modified vaccines in Europe Primary Objective: To determine whether there is an increased risk of pre-specified AESIs following the administration of the Pfizer-BioNTech COVID- 19 bivalent Omicron-modified vaccine compared with not receiving any COVID-19 bivalent vaccine, in individuals who received a complete primary series of any COVID-19 monovalent vaccine

Action: For adoption of advice to CHMP

7.2.23. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 064.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for a non-interventional post-approval safety study of Pfizer-BioNTech Bivalent COVID-19 Vaccine in the United States to ensure comprehensive understanding of real-world safety of the Pfizer-BioNTech COVID-19 bivalent Omicron-modified vaccine in large samples of general US populations. (category 3 study in the RMP v9.1 submitted within procedure X-176 and II-177-G)

Action: For adoption of advice to CHMP

7.2.24. Vutrisiran - AMVUTTRA (CAP) - EMEA/H/C/005852/MEA 002.1

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002 [protocol amendment for study ALN-TTR02-013, ConTTRibute Study: global, prospective, observational, multicentre long-term study. This is a prospective, observational study that will provide a robust assessment of the long-term safety of Amvuttra in real-world clinical practice along with a comparator group being enrolled in ConTTRibute who follow local standard of care. ConTTRibute aims to document the natural history, clinical characteristics, and management of ATTR amyloidosis as part of routine clinical care. The study cohort will include patients with hATTR amyloidosis under care at the participating study site, as no exclusion criteria are intended with this observational cohort. Patients with hepatic impairment will be observed as part of the cohort. The study will also include data collection on the clinical consequences of vitamin A deficiency, including delayed symptoms, and pregnancy exposure and pregnancy and infant outcomes] as per the request for supplementary information (RSI) adopted in March 2023

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[17]

7.3.1. Chlormadinone acetate, ethinyl estradiol (NAP) - EMEA/H/N/PSR/J/0042

Applicant: GEDEON RICHTER Plc

PRAC Rapporteur: Martin Huber

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

Scope: Final study report for: risk of venous thromboembolism – The role of oral contraceptives – a case control study comparing levonorgestrel and chlormadinone acetate to compare the VTE risk of combined oral contraceptives (COCs) containing CMA 2mg / ethinylestradiol (EE) 30 µg, compared to COCs containing levonorgestrel (LNG) 0.15mg, both combined with 30 µg ethinylestradiol (EE)

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

7.3.2. Roflumilast – DAXAS (CAP) - EMEA/H/C/PSR/S/0041

Applicant: AstraZeneca AB

PRAC Rapporteur: Monica Martinez Redondo

Scope: Final study report for a long-term post-marketing observational study of the safety of roflumilast

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

7.3.3. Valproate[18] (NAP) - EMEA/H/N/PSR/J/0036

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Survey among HCP to assess knowledge of HCP and behaviour with regards to pregnancy prevention programme (PPP) as well as receipt/use of DHPC and educational materials and survey among patients to assess knowledge of the patients with regards to PPP as well as receipt/use of educational materials

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[19]

7.4.1. Cangrelor - KENGREXAL (CAP) - EMEA/H/C/003773/II/0031

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final report from study ARCANGELO (itAlian pRospective study on CANGrELOr), listed as a category 3 study in the RMP. This is a multicentre observational, prospective cohort study including patients with acute coronary syndromes undergoing percutaneous coronary intervention who receive cangrelor i.v. transitioning to either clopidogrel, prasugrel or ticagrelor per os. The primary objective is to assess the safety of cangrelor in a real-world setting, when administered in patients with acute coronary syndromes undergoing percutaneous coronary intervention (PCI). The safety of cangrelor is

[18] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium
[19] 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

based on the incidence of any haemorrhage at 30 days post-PCI. The RMP version 5.1 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.2. Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/II/0032

Applicant: Almirall S.A

PRAC Rapporteur: Mari Thorn

Scope: Submission of the final report from study M-41008-44 listed as a category 3 study in the RMP. This is a non-interventional PASS titled 'A retrospective chart review to assess the effectiveness of the Skilarence risk minimisation activities in daily practice'. The RMP version 2.1 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.3. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0082

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.6 of the SmPC in order to update information on pregnancy based on results from study 109MS402 - Tecfidera (dimethyl fumarate) Pregnancy Exposure Registry, listed as a category 3 study in the RMP; this is an observational study and aims to address the safety concern of effects on pregnancy outcome and prospectively evaluates pregnancy outcomes in women with MS who were exposed to a Registry-specified Biogen MS product during the eligibility window for that product. The package leaflet is updated accordingly. The RMP version 15.1 has also been submitted. In addition, the MAH has taken the opportunity to introduce editorial changes to the product information

Action: For adoption of PRAC Assessment Report

7.4.4. Fenofibrate, pravastatin sodium - PRAVAFENIX (CAP) - EMEA/H/C/001243/II/0034

Applicant: Laboratoires SMB s.a.

PRAC Rapporteur: Nathalie Gault

Scope: Submission of the final report from study POSE: Pravafenix Observational Study in Europe (EUPAS 13661), listed as a category 3 study in the RMP (MEA/007.10). This is an observational, three-year cohort comparative study on the safety of the fixed dose combination pravastatin 40 mg/ fenofibrate 160 mg (Pravafenix) versus statin alone in real clinical practice

Action: For adoption of PRAC Assessment Report

7.4.5. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA 004.14

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual report for the passive enhanced safety surveillance (ESS) D2560C00008: a post-marketing non-interventional cohort study of the safety of live attenuated influenza vaccine (LAIV) in subjects 2 through 17 years of age for the 2021-2022 influenza season. The ESS should be repeated during the vaccination campaign for the flu season 2022-2023. After that, safety surveillance will continue passively and safety data will be discussed through PSURs. The RMP will be updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/II/0070

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 105MS401. The objective of this study was to determine the incidence of serious adverse events (SAEs) in patients with relapsing forms of MS in routine clinical practice and to assess the overall long-term clinical effectiveness of peginterferon beta-1a in patients with relapsing forms of MS in routine clinical practice

Action: For adoption of PRAC Assessment Report

7.4.7. Radium (Ra^{223}) - XOFIGO (CAP) - EMEA/H/C/002653/II/0052

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Submission of the final report from study 20702 listed as a category 3 study in the RMP. This is a non-interventional drug utilisation study to investigate the risk of off-label use

Action: For adoption of PRAC Assessment Report

7.4.8. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0052

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final report from study A3921334 listed as a category 3 study in the RMP. This is a Non-Interventional PASS to evaluate the effectiveness of additional risk minimisation measures materials for tofacitinib in Europe via a survey of healthcare professionals

Action: For adoption of PRAC Assessment Report

7.4.9. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0100

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of section 4.6 of the SmPC in order to update information on pregnancy based on the final synoptic report from study CNTO1275PSO4037 (OTIS); this is a

pregnancy exposure registry for Stelara. The package leaflet is updated accordingly. The RMP version 26.2 has also been submitted

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. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/MEA 022

Applicant: Bayer AG

PRAC Rapporteur: Nathalie Gault

Scope: Two-year interim study report for FIREFLEYE NEXT Study # 20275: An extension study to evaluate the long-term outcomes of subjects who received teatment for retinopathy of prematurity in Study 20090

Action: For adoption of advice to CHMP

7.5.2. Beclometasone, formoterol, glycopyrronium bromide - TRIMBOW (CAP) - EMEA/H/C/004257/MEA 002.4

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Second progress report for study CLI-05993BA1-05 (TRIBE): a multinational database cohort study to assess adverse cardiovascular and cerebrovascular outcomes in patients with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurized metered dose inhaler (pMDI)

Action: For adoption of advice to CHMP

7.5.3. Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - RIARIFY (CAP) - EMEA/H/C/004836/MEA 002

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: First and second progress reports for study CLI-05993BA1-05 (TRIBE): a multinational database cohort study to assess adverse cardiovascular and cerebrovascular outcomes in patients with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurized metered dose inhaler (pMDI)

Action: For adoption of advice to CHMP

7.5.4. Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - TRYDONIS (CAP) - EMEA/H/C/004702/MEA 002

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: First and second progress reports for study CLI-05993BA1-05 (TRIBE): a multinational database cohort study to assess adverse cardiovascular and cerebrovascular outcomes in patients with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurized metered dose inhaler (pMDI)

Action: For adoption of advice to CHMP

7.5.5. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 005.1

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: First interim report for study 2019nCoV-405: Global Safety Surveillance Study of Pregnancy and Infant Outcomes Study Using C-VIPER. A registry-based observational cohort safety surveillance study to characterise the population of pregnant women who are vaccinated with Nuvaxovid, estimate the frequency of selected adverse pregnancy outcomes in women and selected adverse foetal/neonatal/infant outcomes at birth and up to the first 12 months of life of infants from pregnancies in women who received Nuvaxovid during pregnancy

Action: For adoption of advice to CHMP

7.5.6. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 006.3

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: Interim report for study EP0220 (old ZX008-2104): A European Study of the Effectiveness of Risk Minimisation Measures for Fenfluramine in Dravet Syndrome (interim analysis) (EUPAS48741) ; Cross-sectional, multicountry, noninterventional survey conducted through an anonymous web questionnaire among physicians who prescribe fenfluramine in European countries

Action: For adoption of advice to CHMP

7.5.7. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/MEA 029.4

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 029.3 [Updated protocol for study Instanyl-5002 (listed as a category 3 study in the RMP): a non-interventional study to assess the effectiveness of

updated educational materials on prescribers' knowledge and behaviour with respect to risks associated with Instanyl (fentanyl) off-label use together with an interim report and the statistical analysis plan (SAP)] as per request for supplementary information (RSI) adopted in March 2023 together with an interim report for study Instanyl-5002

Action: For adoption of advice to CHMP

7.5.8. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 012.12

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Twelfth annual interim report for study D2404 of the Pregnancy Intensive Monitoring program (PRIM)

Action: For adoption of advice to CHMP

7.5.9. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 038.6

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 038.5 [Third interim report for study CFTY720D2311: a two-year, double-blind, randomised, multicentre, active-controlled core phase study to evaluate the safety and efficacy of fingolimod administered orally once daily versus interferon β-1a intramuscular (IM) once weekly in paediatric patients with multiple sclerosis with five-year fingolimod extension phase] as per the request for supplementary information (RSI) adopted in March 2023

Action: For adoption of advice to CHMP

7.5.10. Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/MEA 002.2

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Jo Robays

Scope: Third annual report for study ACE-536-LTFU-001: a study to evaluate the long-term safety, including thromboembolic events (TEEs) and progression to acute myeloid leukaemia (AML) and/or other malignancies/pre malignancies of luspatercept in patients who have participated in company-sponsored luspatercept clinical trials

Action: For adoption of advice to CHMP

7.5.11. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.12

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Progress report for study A-LUT-T-E02-402 (SALUS): an international, non-interventional, post-authorisation long-term safety study of Lutathera (lutetium (177Lu)

oxodotreotide) in patients with unresectable or metastatic, well-differentiated, somatostatin receptor positive, gastroenteropancreatic neuroendocrine tumours

Action: For adoption of advice to CHMP

7.5.12. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.14

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Final progress report for study D3820R00009 [Naloxegol Health Outcomes PASS – An observational PASS of MOVENTIG (Naloxegol) Among Patients Aged 18 Years and Older Diagnosed with Non- Cancer Pain and Cancer Pain and Treated with Opioids Chronically in Selected European Populations.]

Action: For adoption of advice to CHMP

7.5.13. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 005.5

Applicant: Bayer AG

PRAC Rapporteur: Gabriele Maurer

Scope: Annual report for study 15689: evaluation of AEs of special interest in the PedNet registry (European Paediatric Network for Haemophilia Management) (Epidemiological Study)

Action: For adoption of advice to CHMP

7.5.14. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 004.6

Applicant: Bayer AG

PRAC Rapporteur: Gabriele Maurer

Scope: MAH's response to MEA 004.5 [Thirteenth annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry] as per the request for supplementary information (RSI) adopted in April 2023

Action: For adoption of advice to CHMP

7.5.15. Ponesimod - PONVORY (CAP) - EMEA/H/C/005163/MEA 001.3

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: First annual progress report for study POEM: PASS: Ponesimod Pregnancy Outcomes Program Utilizing Enhanced Pharmacovigilance Monitoring

Action: For adoption of advice to CHMP

7.5.16. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/MEA 002.4

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Second annual interim report for study CBAF312A2411 (listed as category 3 study in the RMP): evaluation of pregnancy and infant outcomes in Mayzent patients using pregnancy outcomes intensive monitoring (PRIM)

Action: For adoption of advice to CHMP

7.5.17. Sutimlimab - ENJAYMO (CAP) - EMEA/H/C/005776/MEA 003

Applicant: Sanofi B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Annual interim report for study OBS16454: Cold Agglutinin Disease Real World Evidence Registry (CADENCE)

Action: For adoption of advice to CHMP

7.5.18. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.7

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 003.6 [Third annual progress report for study M14745-40 (Tildrakizumab PASS in European Psoriasis Registry): To collect long-term safety data in particular relating to event of special interest (important potential risks and pregnancy related outcomes) for tildrakizumab (Malignancies, MACEs, Serious infections, SIBH, Hypersensitivity, IBD, Safety in pregnant and lactating women). To further characterise the long-term safety profile of tildrakizumab in the treatment of psoriasis under conditions of routine clinical care] as per the request for supplementary information (RSI) adopted in March 2023

Action: For adoption of advice to CHMP

7.5.19. Zanamivir - DECTOVA (CAP) - EMEA/H/C/004102/MEA 003.2

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual update on the observational pregnancy registry study 201840 (listed as category 3 study in the RMP)

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/ANX 009.3

Applicant: Sanofi Belgium

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: MAH's responses to ANX 009.2 [The provision of answers to questions about the feasibility report of the noninterventional PASS to investigate the risk of mortality in multiple sclerosis (MS) patients treated with alemtuzumab (Lemtrada) relative to comparable MS patients using other disease modifying treatments (DMTs)] as per request for supplementary information (RSI) adopted in May 2023

Action: For adoption of advice to CHMP

7.6.2. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 018

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Feasibility assessment for the filgotinib drug utilization studies in rheumatoid arthritis (GLPG0634-CL-408) and ulcerative colitis (GLPG0634-CL-417) within European registries

Action: For adoption of advice to CHMP

7.6.3. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 009.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Justification for early termination of study C4591011: Assessment of occurrence of safety events of interest, including severe or atypical COVID-19 in a cohort of people within the Department of Defense Healthcare System (Study C4591011)

Action: For adoption of advice to CHMP

7.6.4. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 047.3

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope MAH's response to MEA 047.2 [Initial statistical analysis plan (SAP) for study C4591038 (listed as a category 3 study in the RMP): a post conditional approval active surveillance study among individuals in Europe receiving the Pfizer BioNTech coronavirus disease 2019 (COVID-19) vaccine to investigate natural history of post-vaccination myocarditis and pericarditis] as per the request for supplementary information (RSI) adopted in March 2023

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Evinacumab - EVKEEZA (CAP) - EMEA/H/C/005449/S/0010 (without RMP)

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thorn

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Tecovirimat - TECOVIRIMAT SIGA (CAP) - EMEA/H/C/005248/S/0004 (with RMP)

Applicant: SIGA Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/R/0071 (without RMP)

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Loncastuximab tesirine - ZYNLONTA (CAP) - EMEA/H/C/005685/R/0009 (without RMP)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Jirsová

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0042 (without RMP)

Applicant: Advanz Pharma Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Sotorasib - LUMYKRAS (CAP) - EMEA/H/C/005522/R/0012 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.5. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/R/0035 (without RMP)

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Adalimumab - IDACIO (CAP) - EMEA/H/C/004475/R/0022 (without RMP)

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Bevacizumab - ZIRABEV (CAP) - EMEA/H/C/004697/R/0029 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/R/0044 (without RMP)

Applicant: TEVA GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Lusutrombopag - MULPLEO (CAP) - EMEA/H/C/004720/R/0018 (without RMP)

Applicant: Shionogi B.V.

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Macimorelin - GHRYVELIN (CAP) - EMEA/H/C/004660/R/0020 (without RMP)

Applicant: Consilient Health Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Miglustat - MIGLUSTAT DIPHARMA (CAP) - EMEA/H/C/004904/R/0019 (without RMP)

Applicant: DIPHARMA Arzneimittel GmbH

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Naldemedine - RIZMOIC (CAP) - EMEA/H/C/004256/R/0023 (without RMP)

Applicant: Shionogi B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. 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

8.3.9. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/R/0039 (without RMP)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Silodosin - SILODOSIN RECORDATI (CAP) - EMEA/H/C/004964/R/0012 (without RMP)

Applicant: Recordati Ireland Ltd

PRAC Rapporteur: Valentina Di Giovanni

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

None

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. Vote by proxy

None

12.1.3. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q2 2023

Action: For information

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

12.7.1. PRAC work plan 2023 – update

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q2 2023 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q2 2023

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla**Action:** For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.12.4. Specific adverse drug reaction (ADR) follow up questionnaire (FUQ) – update on the activities of the drafting group

PRAC lead: Tiphaine Vaillant

Action: For discussion

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.14.3. Risk management plan (RMP) of medicinal product(s) – update on the process of publication on EMA website

Action: For adoption

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

12.20.1. Revised process for prioritisation and regulatory follow-up of impact research (Rev.2)

Action: For discussion

12.21. Others

12.21.1. Guideline on clinical investigation of recombinant and human plasma-derived factor IX products and core SmPC – revision

Action: For discussion

12.21.2. Patient Experience Data (PED) – priority activities and actions

Action: For discussion

13. Any other business

Next meeting on: 25-28 September 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.

For a list of acronyms and abbreviations, see:
List of abbreviations used in EMA human medicines scientific committees and CMDh documents, and in

relation to EMA's regulatory activities

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