11 April 2023
EMA/PRAC/120400/2023
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 11-14 April 2023

Chair: Sabine Straus – Vice-Chair: Martin Huber

11 April 2023, 13:00 – 19:30, room 1C / via teleconference

12 April 2023, 08:30 – 19:30, room 1C / via teleconference

13 April 2023, 08:30 – 19:30, room 1C / via teleconference

14 April 2023, 08:30 – 16:00, room 1C / via teleconference

Organisational, regulatory and methodological matters (ORGAM)

26 April 2023, 09:00 - 12:00, via teleconference

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 11-14 April 2023. See April 2023 PRAC minutes (to be published post May 2023 PRAC meeting).

1.2. Agenda of the meeting on 11-14 April 2023

Action: For adoption

1.3. Minutes of the previous meeting on 13-16 March 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

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Acetazolamide (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of choroidal effusion and choroidal detachment

Action: For adoption of PRAC recommendation

EPITT 19924 – New signal

Lead Member State(s): SE

4.1.2. Apalutamide – ERLEADA (CAP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Signal of interstitial lung disease (ILD)

Action: For adoption of PRAC recommendation

EPITT 19911 – New signal

Lead Member State(s): FR

4.1.3. Enoxaparin – INHIXA (CAP)

Applicant: Techdow Pharma

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

PRAC Rapporteur: Menno van der Elst

Scope: Signal of angiokeratoma

Action: For adoption of PRAC recommendation

EPITT 19909 – New signal

Lead Member State(s): NL

4.1.4. Megestrol (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of meningioma

Action: For adoption of PRAC recommendation

EPITT 19923 – New signal

Lead Member State(s): IE

4.1.5. Pramipexole[3] – MIRAPEXIN (CAP); OPRYMEA (CAP); PRAMIPEXOLE TEVA (CAP); SIFROL (CAP); (NAP)

Applicant(s): Boehringer Ingelheim International GmbH (Mirapexin, Sifrol), KRKA, d.d., Novo mesto (Oprymea), Teva B.V. (Pramipexole Teva), various

PRAC Rapporteur: To be appointed

Scope: Signal of intestinal obstruction

Action: For adoption of PRAC recommendation

EPITT 19898 – New signal

Lead Member State(s): DK, SE

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/SDA/113

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of pemphigus and pemphigoid

Action: For adoption of PRAC recommendation

[3] Prolonged release tablets

EPITT 19858 – Follow-up to December 2022[4]

4.3.2. Elasomeran – SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/081

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of pemphigus and pemphigoid

Action: For adoption of PRAC recommendation

EPITT 19860 – Follow-up to December 2022[5]

4.3.3. Evolocumab – REPATHA (CAP) - EMEA/H/C/003766/SDA/017

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of weight increase and abnormal weight gain

Action: For adoption of PRAC recommendation

EPITT 19867 – Follow-up to December 2022[6]

4.3.4. Glucagon-like peptide-1 (GLP-1) receptor agonists: dulaglutide – TRULICITY (CAP); exenatide – BYDUREON (CAP), BYETTA (CAP); insulin degludec, liraglutide – XULTOPHY (CAP); liraglutide – SAXENDA (CAP), VICTOZA (CAP); insulin glargine, lixisenatide – SULIQUA (CAP); lixisenatide - LYXUMIA (CAP); semaglutide – OZEMPIC (CAP), RYBELSUS (CAP), WEGOVY (CAP)

Applicant: AstraZeneca AB (Bydureon, Byetta), Eli Lilly Nederland B.V. (Trulicity), Novo Nordisk A/S (Ozempic, Rybelsus, Saxenda, Victoza, Wegovy, Xultophy), Sanofi Winthrop Industrie (Lyxumia, Suliqua)

PRAC Rapporteur: Mari Thorn

Scope: Signal of thyroid cancer

Action: For adoption of PRAC recommendation

EPITT 18292 – Follow up to January 2023

4.3.5. Tozinameran – COMIRNATY (CAP) - EMEA/H/C/005735/SDA/061

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of pemphigus and pemphigoid

Action: For adoption of PRAC recommendation

EPITT 19859 – Follow-up to December 2022[7]

[4] Held 28 November - 01 December 2022
[5] Held 28 November - 01 December 2022
[6] Held 28 November - 01 December 2022

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. Degarelix acetate - EMEA/H/C/006048

Scope : Treatment of prostate cancer

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

5.1.2. Natalizumab - EMEA/H/C/005752

Scope : Treatment of active relapsing remitting multiple sclerosis (RRMS)

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

5.1.3. Pegfilgrastim - EMEA/H/C/005587

Scope : Treatment of neutropenia

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

5.1.4. Respiratory syncytial virus vaccines - EMEA/H/C/006027

Scope accelerated assessment): Prevention of respiratory tract disease

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

5.1.5. Talquetamab - EMEA/H/C/005864, PRIME, Orphan

Applicant: Janssen-Cilag International N.V.

Scope accelerated assessment): Monotherapy treatment of adult patients with relapsed and refractory multiple myeloma

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. Efavirenz - STOCRIN (CAP) - EMEA/H/C/000250/II/0130

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

[7] Held 28 November - 01 December 2022

Scope: Submission of an updated RMP version 9.0 including removal of all safety concerns in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

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

Applicant: Zogenix ROI Limited

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

5.2.3. Palivizumab - SYNAGIS (CAP) - EMEA/H/C/000257/II/0131

Applicant: AstraZeneca AB

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of an updated RMP version 2.0 in order to remove from the list of safety concerns "Anaphylaxis, Anaphylactic shock, and Hypersensitivity" and "Medication error of mixing lyophilised and liquid palivizumab before injection". In addition, the MAH took the opportunity to apply the revised template

Action: For adoption of PRAC Assessment Report

5.2.4. Somatropin - NUTROPINAQ (CAP) - EMEA/H/C/000315/II/0077

Applicant: Ipsen Pharma

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP version 4.0 in order to remove some of the safety concerns in compliance with GVP Module V Revision 2. In addition, the MAH took the opportunity to add data from final clinical study report of International Cooperative Growth Study (iNCGS) registry (non-interventional study) and exposure and safety information

Action: For adoption of PRAC Assessment Report

5.2.5. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/WS2402/0069; MODIGRAF (CAP) - EMEA/H/C/000954/WS2402/0045

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eamon O'Murchu

Scope: Submission of an updated RMP (version 4) to reflect the new Transplant Pregnancy Registry International (TPRI) final study submission milestone, related to procedure EMEA/H/C/000712/MEA030 and EMEA/H/C/000954/MEA022 (Study F506-PV-0001), from 21 December 2021 to 30 June 2023

Action: For adoption of PRAC Assessment Report

5.2.6. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0059

Applicant: Amgen Europe B.V., ATMP[8]

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of an updated RMP version 10 in order to update and reclassify identified risk of 'disseminated herpetic infection' based on the cumulative assessment of literature review and MAH Global Safety Database and to remove studies 20180062 and 20180099 from Planned and Ongoing Studies from the list of Pharmacovigilance Plan studies in the Annex II

Action: For adoption of PRAC Assessment Report

5.2.7. 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

5.2.8. Tobramycin - TOBI PODHALER (CAP) - EMEA/H/C/002155/II/0053, Orphan

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP version 8.0 following PSUR single assessment (PSUSA) procedure (PSUSA/00009315/202106) concluded in February 2022 in order to update it based on the guidance provided in the GVP and to remove the safety concerns as well as to reflect the finalisation of study CTBM100C2407 and the transfer of ownership

Action: For adoption of PRAC Assessment Report

5.2.9. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/II/0061

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 12 in order to remove certain risks from the list of safety concerns

[8] Advanced therapy medicinal product

Action: For adoption of PRAC Assessment Report

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

5.3.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0094

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Update of section 4.2 of the SmPC in order to add home infusion upon request by PRAC following the assessment of PSUSA/00000086/202109 based on a cumulative search of the MAH Global Pharmacovigilance database and literature. The package leaflet and Annex II are updated accordingly. The RMP version 10.0 has also been submitted

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

5.3.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0095

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Update of sections 4.4 and 5.2 of the SmPC in order to update warning on immunogenicity. 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

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/0077/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Grouped application comprising two type II variations as follows: 1) Update of sections 4.2, 4.4. and 4.8 of the SmPC in order to add dose modification advice and new warning for two new important identified risks of immune-mediated myelitis and immune-mediated facial paresis and to add facial paresis and myelitis to the list of adverse drug reactions (ADRs) with frequency Rare following a safety signal based on the cumulative review of the MAH safety database and literature search; 2) Update of section 4.8 of the SmPC in order to add dry mouth to the list of adverse drug reactions (ADRs) with frequency Common, based on the results from study WO39210 (IMmotion010), a multicenter, randomised, placebo-controlled, double-blind study evaluating the efficacy and safety of atezolizumab versus placebo in patients with renal cell carcinoma (RCC) who are at high risk of disease recurrence following resection.
The Annex II and package leaflet are updated accordingly. The RMP version 26.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the SmPC and to update the list of local representatives in the package leaflet

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

5.3.4. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/II/0022, Orphan

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations and to update pharmacokinetic information for use in patients with severe hepatic impairment based on the final results from study BLU-285-0107 listed as a category 3 study in the RMP; this is a phase 1, open-label, single-dose study to investigate the influence of severe hepatic impairment on the pharmacokinetics of avapritinib. The package leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template version 10.3

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

5.3.5. 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

5.3.6. Azacitidine - AZACITIDINE ACCORD (CAP) - EMEA/H/C/005147/X/0013

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Menno van der Elst

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (10 mg/ml powder for solution for infusion) and a new route of administration (intravenous use). The RMP version 2 is updated in accordance

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

5.3.7. Casirivimab, imdevimab - RONAPREVE (CAP) - EMEA/H/C/005814/II/0002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of coronavirus (COVID-19) in hospitalised patients in adults and adolescents aged 12 years and older weighing at least 40 kg. As a consequence, sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated.

The package leaflet, the labelling and the RMP (version 1.1) are updated in accordance

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

5.3.8. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS2421/0059; FORXIGA (CAP) - EMEA/H/C/002322/WS2421/0080

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Submission of final results from non-clinical mechanistic model studies listed as a category 3 PASS in the RMP. These are non-clinical studies aiming to further investigate underlying mechanisms of diabetes ketoacidosis (DKA) in association with dapagliflozin. The RMP version 29 has also been submitted

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

5.3.9. Ebola Zaire vaccine (live, attenuated) - ERVEBO (CAP) - EMEA/H/C/004554/II/0025

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the paediatric population from 1 year to less than 18 years of age based on final results from study V920-016 (PREVAC); this is a phase 2, randomised, double-blind, placebo-controlled study of 2 leading Ebola vaccine candidates (Ad26.ZEBOV/MVA-BN-Filo and V920) and 3 vaccine strategies (Ad26.ZEBOV/MVABN-Filo, 1-dose V920, and 2 dose V920) to evaluate immunogenicity and safety in healthy children and adolescents from 1 to 17 years of age and adults 18 years of age and older. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.3 of the SmPC are updated. The package leaflet is updated in accordance. Version 1.2 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the Annex II and the list of local representatives in the package leaflet

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

5.3.10. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0097/G

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Grouped variation consisting of : 1) Extension of indication to include a 25 µg booster dose of Spikevax bivalent Original/Omicron BA.4-5 (12.5 µg elasomeran /12.5 µg davesomeran) in children aged 6 through 11 years of age; as a consequence, sections 2, 4.1, 4.2, 4.4, and 6.6 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. Version 6.5 of the RMP has also been submitted; 2) Update of sections 4.8 and 5.1 of the Spikevax bivalent Original/Omicron BA.1 SmPC to add median follow-up period and D91 persistence data, based on Parts F and G (mRNA- 1273.214) of study mRNA-1273-P205 (NCT04927065), an open-label Phase 2/3 study evaluating the immunogenicity and safety of variant-targeting booster candidate vaccines. The package leaflet is updated accordingly; 3) Update sections 4.8 and 5.1 of the Spikevax bivalent Original/Omicron BA.4-5 SmPC to add ADR details and clinical data, based on Part H

(mRNA- 1273.222) of study mRNA-1273-P205 (NCT04927065), an open-label Phase 2/3 study evaluating the immunogenicity and safety of variant-targeting booster candidate vaccines. In addition, the Marketing authorisation holder took the opportunity to implement a number of editorial changes to the product information

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

5.3.11. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/II/0076

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication for JARDIANCE to include treatment of children aged 10 years and above with type 2 diabetes based on results from study DINAMO 1218-0091; this is a double-blind, randomised, placebo-controlled, parallel group trial to evaluate the efficacy and safety of empagliflozin and linagliptin over 26 weeks, with a double-blind active treatment safety extension period up to 52 weeks, in children and adolescents with type 2 diabetes mellitus. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 21.0 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. Follitropin delta - REKOVELLE (CAP) - EMEA/H/C/003994/II/0037/G

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Menno van der Elst

Scope: Grouped application consisting of: 1) Update of sections 4.1, 4.2, 4.4, 4.5 and 5.1 of the SmPC to update the safety information following final results from study 000304 (BEYOND). This is a randomised, controlled, open label, parallel group, multicentre trial comparing the efficacy and safety of individualised FE 999049 (follitropin delta) dosing, using a long gonadotropin-releasing hormone (GnRH) agonist protocol and a GnRH antagonist protocol in women undergoing controlled ovarian stimulation; 2) Update of section 4.8 of the SmPC, including the tabulation of adverse drug reactions based on pooled safety data from studies ESTHER-1, ESTHER-2, 000273, 000145, BEYOND and RAINBOW. The updated RMP version 8.0 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

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

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of: 1) update of section 5.3 of the SmPC based on final results from study AS1-GLP18-007 listed as a category 3 study in the RMP: a 104-week subcutaneous injection carcinogenicity study in Sprague Dawley rats; 2) update of section 5.3 of the SmPC based on final results from study AS1-GLP18-004: a 26-week subcutaneous injection carcinogenicity study in TgRasH2 mice. The RMP version 2.1 has also

been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.14. Hydroxycarbamide - XROMI (CAP) - EMEA/H/C/004837/II/0019

Applicant: Nova Laboratories Ireland Limited

PRAC Rapporteur: Jo Robays

Scope: Extension of indication to include the prevention of vaso-occlusive complications of sickle cell disease in children from 6 months to 2 years of age for Xromi, based on final results from the paediatric study INV543, listed as a category 3 study in the RMP; this is a single-arm, open-label, multi-center study in children with sickle cell anaemia over 6 months of age. 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 4.1 of the RMP has also been submitted

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

5.3.15. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0100

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include in combination with nivolumab the treatment of adolescents (12 years of age and older) for advanced (unresectable or metastatic) melanoma, based on the pivotal study CA209070; this is a multicentre, open-label, single arm, phase 1/2 trial of nivolumab +/- ipilimumab in children, adolescents and young adults with recurrent or refractory solid tumours or lymphomas. 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 38.0 of the RMP has also been submitted

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

5.3.16. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/X/0114/G

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Extension application to add a new strength (59.5 mg) of the granules pharmaceutical form grouped with a type II variation to support a new indication in a combination regimen with ivacaftor/tezacaftor/elexacaftor 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 RMP (version 15.1) has also been submitted. Type IB B.II.f.1.b - to extend the shelf-life of the granules pharmaceutical form of the finished product as packaged for sale from 3 to 4 years. The product information has been updated accordingly

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/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

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

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

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

5.3.19. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/II/0052

Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: Update of section 4.8 of the SmPC based on pooled safety data including results of Study 307, an ongoing, multicentre, randomised, open-label study that is being conducted to compare the efficacy and safety of lenvatinib in combination with everolimus or pembrolizumab versus sunitinib as first-line (1L) treatment in adults with advanced renal cell carcinoma (RCC). The provision of the clinical study report (CSR) addresses the post-authorisation measure MEA/FSR 009.3. The package leaflet is updated accordingly. An updated RMP version 15.0 has been submitted

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

5.3.20. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/X/0078/G

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped application consisting of: 1) Extension application to add a new strength of 75 mg of lumacaftor and 94 mg of ivacaftor fixed dose combination granules; 2) Extension of indication to include treatment of cystic fibrosis for children aged 1 to less than 2 years old of age who are homozygous for the F508del mutation in the CFTR gene, based on final results from study 122, a 2-part study of cystic fibrosis (CF) subjects 1 to <2 years of age homozygous for F508del. As a consequence, sections 4.1, 4.2, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 11.2 of the RMP has also been submitted

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

5.3.21. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/II/0039

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC in order to update information regarding the use of naloxegol in opioid-induced constipation (OIC) patients with cancer-related pain based on real-world data from non-interventional studies (NACASY, KYONAL, and MOVE studies), post-marketing data, and literature. The package leaflet is updated accordingly. The RMP version 8 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

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

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

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

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

5.3.23. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0125/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include adolescent patients aged 12 years and older in treatment of advanced (unresectable or metastatic) melanoma (nivolumab monotherapy), treatment of advanced (unresectable or metastatic) melanoma (nivolumab in combination with ipilimumab) and adjuvant treatment of melanoma (nivolumab monotherapy) for Opdivo, based on results from a nonclinical biomarker study (Expression of PD-L1 (CD274), and characterization of tumour infiltrating immune cells in tumours of paediatric origin), also based on results from a Phase 1/2 clinical study (CA209070, a phase 1/2 study of Nivolumab (Ind# 124729) in children, adolescents, and young adults with recurrent or refractory solid tumours as a single agent and in combination with Ipilimumab) and a modelling and simulation study. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. Version 30.0 of the RMP has also been submitted

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

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Monica Martinez Redondo

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

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

5.3.25. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/II/0064, Orphan

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of newly diagnosed adult patients with Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL), either with Iclusig (ponatinib) in combination with chemotherapy, or with Iclusig (ponatinib) monotherapy after corticosteroid induction in patients not eligible to receive chemotherapy-based regimens, based on final results from studies AP24534-11-001 and INCB 84344-201. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 22 of the RMP has also been submitted

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

5.3.26. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/II/0037

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of pulmonary arterial hypertension (PAH) in paediatric patients aged 6 to less than 18 years of age with WHO Functional Class (FC) I to III in combination with endothelin receptor antagonists with or without prostanoids for Adempas (riociguat), based on results from pivotal study PATENT-CHILD (Study 15681); this is a Phase III, Open-label, individual dose titration study to evaluate safety, tolerability and pharmacokinetics of riociguat in children from 6 to less than 18 years of age with PAH; As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The package Leaflet is updated in accordance. Version 8.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (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

5.3.27. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/II/0020

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add "Progressive multifocal leukoencephalopathy (PML)" to the list of adverse drug reactions (ADRs) with frequency "not know" based on post-marketing data. The Annex II (Physician's Checklist), and package leaflet are updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to update the text regarding herpes viral infection in the package leaflet in alignment with the currently approved SmPC

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

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

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Marie Louise Schougaard Christiansen

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

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

5.3.29. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/II/0042

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study EFC11759 listed as a category 3 study in the RMP. This is a two-year, multicentre, randomised, double-blind, placebo-controlled, parallel group trial to evaluate efficacy, safety, tolerability and pharmacokinetics of teriflunomide administered orally once daily in paediatric patients with relapsing forms of multiple sclerosis (MS) followed by an open-label extension. The RMP version 8.0 has also been submitted

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

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

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

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

5.3.31. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0114

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of new indication for slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) for RoActemra, based on final results from the pivotal Phase III Study WA29767 (focuSSced) entitled, "A Phase III, Multicenter, Randomised, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Efficacy and Safety of Tocilizumab Versus Placebo in Patients With Systemic Sclerosis" and the supportive Phase II/III Study WA27788 (faSScinate) entitled, "A Phase II/III, Multicenter, Randomised, Double-blind, Placebo-controlled Study To Assess The Efficacy And Safety Of Tocilizumab Versus Placebo In Patients With Systemic Sclerosis". As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 28 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. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0096

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of section 5.1 of the SmPC in order to update information with the 4-year clinical data in patients with ulcerative colitis based on the final report from study CNTO1275UCO3001 listed as a category 3 study in the RMP; this is a phase 3, randomised, double blind, placebo-controlled, parallel-group, multicenter study to evaluate the safety and efficacy of ustekinumab induction and maintenance therapy in subjects with moderately to severely active ulcerative colitis. The RMP version 23.1 has also been submitted. In addition, the MAH took the opportunity to introduce a correction to the product information

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

5.3.33. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/II/0009

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study BGB-3111-113 - A Drug-Drug Interaction Study of Zanubrutinib with Moderate and Strong CYP3A Inhibitors in Patients With B-Cell Malignancies, listed as a category 3 study in the RMP. The RMP version 3.0 has also been submitted

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. Abemaciclib - VERZENIOS (CAP) - PSUSA/00010724/202209

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Abrocitinib - CIBINQO (CAP) - PSUSA/00010976/202209

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alemtuzumab - LEMTRADA (CAP) - PSUSA/00010055/202209

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Amikacin[9] - ARIKAYCE LIPOSOMAL (CAP) - PSUSA/00010882/202209

Applicant: Insmed Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Avacopan - TAVNEOS (CAP) - PSUSA/00010967/202209

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Bedaquiline - SIRTURO (CAP) - PSUSA/00010074/202209

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Bupivacaine, meloxicam - ZYNRELEF (CAP) - PSUSA/00010880/202209

Applicant: Heron Therapeutics, B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Cemiplimab - LIBTAYO (CAP) - PSUSA/00010780/202209

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

[9] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Cenobamate - ONTOZRY (CAP) - PSUSA/00010921/202209

Applicant: Angelini S.p.A.

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Cholic acid[10] - ORPHACOL (CAP) - PSUSA/00010208/202209

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Copper (^{64}Cu) chloride - CUPRYMINA (CAP) - PSUSA/00010040/202208

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

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - PSUSA/00010916/202208

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Dabrafenib - TAFINLAR (CAP) - PSUSA/00010084/202208

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.1.14. Dacomitinib - VIZIMPRO (CAP) - PSUSA/00010757/202209

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Darvadstrocel - ALOFISEL (CAP) - PSUSA/00010676/202209

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

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.16. Duvelisib - COPIKTRA (CAP) - PSUSA/00010939/202209

Applicant: Secura Bio Limited

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Ebola vaccine (rDNA[12], replication-incompetent) - MVABEA (CAP); ZABDENO (CAP) - PSUSA/00010857/202209

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

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Eliglustat - CERDELGA (CAP) - PSUSA/00010351/202208

Applicant: Genzyme Europe BV

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Filgotinib - JYSELECA (CAP) - PSUSA/00010879/202209

Applicant: Galapagos N.V.

[11] Advanced therapy medicinal product
[12] Recombinant deoxyribonucleic acid

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Fremanezumab - AJOVY (CAP) - PSUSA/00010758/202209

Applicant: TEVA GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Galcanezumab - EMGALITY (CAP) - PSUSA/00010733/202209

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Gilteritinib - XOSPATA (CAP) - PSUSA/00010832/202209

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Human alfa1-proteinase inhibitor[13] - RESPREEZA (CAP) - PSUSA/00010410/202208

Applicant: CSL Behring GmbH

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Idebenone[14] - RAXONE (CAP) - PSUSA/00010412/202209

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.1.25. Idecabtagene vicleucel - ABECMA (CAP) - PSUSA/00010954/202209

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP[15]

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.26. Infliximab - FLIXABI (CAP); INFLECTRA (CAP); REMICADE (CAP); REMSIMA (CAP); ZESSLY (CAP) - PSUSA/00010759/202208

Applicant(s): Samsung Bioepis NL B.V. (Flixabi), Pfizer Europe MA EEIG (Inflectra), Janssen Biologics B.V. (Remicade), Celltrion Healthcare Hungary Kft. (Remsima), Sandoz GmbH (Zessly)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Insulin aspart - FIASP (CAP); INSULIN ASPART SANOFI (CAP); KIRSTY (CAP); NOVOMIX (CAP); NOVORAPID (CAP); TRUVELOG MIX 30 (CAP) - PSUSA/00001749/202209

Applicant(s): Sanofi Winthrop Industrie (Insulin aspart Sanofi, Truvelog Mix 30), Mylan IRE Healthcare Limited (Kirsty), Novo Nordisk A/S (Fiasp, NovoMix, NovoRapid)

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Lorlatinib - LORVIQUA (CAP) - PSUSA/00010760/202209

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Lusutrombopag - MULPLEO (CAP) - PSUSA/00010755/202209

Applicant: Shionogi B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Advanced therapy medicinal product

6.1.30. Mepolizumab - NUCALA (CAP) - PSUSA/00010456/202209

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Naloxegol - MOVENTIG (CAP) - PSUSA/00010317/202209

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Naltrexone, bupropion - MYSIMBA (CAP) - PSUSA/00010366/202209

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Ofatumumab - KESIMPTA (CAP) - PSUSA/00010927/202209

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Olipudase alfa - XENPOZYME (CAP) - PSUSA/00011003/202209

Applicant: Genzyme Europe BV

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Panitumumab - VECTIBIX (CAP) - PSUSA/00002283/202209

Applicant: Amgen Europe B.V.

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Pembrolizumab - KEYTRUDA (CAP) - PSUSA/00010403/202209

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Pitolisant - OZAWADE (CAP); WAKIX (CAP) - PSUSA/00010490/202209

Applicant(s): Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Ponesimod - PONVORY (CAP) - PSUSA/00010940/202209

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Pralsetinib - GAVRETO (CAP) - PSUSA/00010961/202209

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Raltegravir - ISENTRESS (CAP) - PSUSA/00010373/202209

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Rilpivirine[16] - REKAMBYS (CAP) - PSUSA/00010901/202209

Applicant: Janssen-Cilag International N.V.

[16] Intramuscular use only

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Ritonavir - NORVIR (CAP) - PSUSA/00002651/202208

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Selinexor - NEXPOVIO (CAP) - PSUSA/00010926/202209

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Tebentafusp - KIMMTRAK (CAP) - PSUSA/00010991/202209

Applicant: Immunocore Ireland Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Tenecteplase - METALYSE (CAP) - PSUSA/00002888/202208

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Tepotinib - TEPMETKO (CAP) - PSUSA/00010979/202209

Applicant: Merck Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Tildrakizumab - ILUMETRI (CAP) - PSUSA/00010720/202209

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Trabectedin - YONDELIS (CAP) - PSUSA/00003001/202209

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Velmanase alfa - LAMZEDE (CAP) - PSUSA/00010677/202209

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Vemurafenib - ZELBORAF (CAP) - PSUSA/00009329/202208

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Vernakalant hydrochloride - BRINAVESS (CAP) - PSUSA/00003109/202208

Applicant: Correvio

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Budesonide, formoterol - BIRESP SPIROMAX (CAP); BUDESONIDE/FORMOTEROL TEVA PHARMA B.V. (CAP); DUORESP SPIROMAX (CAP); NAP - PSUSA/00010585/202208

Applicant(s): Teva Pharma B.V. (BiResp Spiromax, Budesonide/Formoterol Teva Pharma B.V., DuoResp Spiromax), various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Glycopyrronium[17] - SIALANAR (CAP); NAP - PSUSA/00010529/202209

Applicant(s): Proveca Pharma Limited (Sialanar), various

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Midazolam[18] [19] - BUCCOLAM (CAP); NAP - PSUSA/00010118/202209

Applicant(s): Laboratorios Lesvi S.L. (BUCCOLAM), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Octocog alfa - ADVATE (CAP); KOGENATE BAYER (CAP); KOVALTRY (CAP); NAP - PSUSA/00002200/202208

Applicant(s): Takeda Manufacturing Austria AG (Advate), Bayer AG (KOGENATE Bayer, Kovaltry), various

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[17] Treatment of severe sialorrhea (chronic pathological drooling) indication(s) only
[18] Oromucosal solution
[19] Indicated for the treatment of prolonged, acute, convulsive seizures

6.2.5. Pantoprazole - CONTROLOC CONTROL (CAP); PANTOZOL CONTROL (CAP); SOMAC CONTROL (CAP); NAP - PSUSA/00002285/202208

Applicant(s): Takeda GmbH (CONTROLOC Control, PANTOZOL Control, SOMAC Control), various

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Adenosine (NAP) - PSUSA/00000062/202208

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Allergen for therapy: dermatophagoides pteronyssinus, dermatophagoides farina[20] (NAP) - PSUSA/00010582/202209

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Biperiden (NAP) - PSUSA/00000415/202208

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Choline alfoscerate (NAP) - PSUSA/00010599/202208

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[20] Oromucosal use, products authorised via mutually recognition procedure and decentralised procedure

6.3.5. Dexamfetamine (NAP) - PSUSA/00000986/202209

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Dornase alpha (NAP) - PSUSA/00001164/202209

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Drospirenone, ethinylestradiol (NAP) - PSUSA/00010217/202209

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Fluoxetine (NAP) - PSUSA/00001442/202209

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Fluvastatin (NAP) - PSUSA/00001457/202208

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Human tetanus immunoglobulin (NAP) - PSUSA/00002909/202208

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Midazolam[21] (NAP) - PSUSA/00002057/202209

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Minocycline (NAP) - PSUSA/00002065/202208

Applicant(s): various

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Paricalcitol (NAP) - PSUSA/00002316/202208

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Piperacillin, tazobactam (NAP) - PSUSA/00002425/202209

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Tretinoin[22] (NAP) - PSUSA/00003016/202208

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[21] All pharmaceutical forms and indications apart from oromucosal solution indicated for the treatment of prolonged, acute, convulsive seizures
[22] Topical formulation(s) only

6.3.16. Treosulfan[23] (NAP) - PSUSA/00009319/202208

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

None

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Fondaparinux sodium - ARIXTRA (CAP) - EMEA/H/C/000403/II/0087

Applicant: Mylan Ire Healthcare Limited

PRAC Rapporteur: Mari Thorn

Scope: To update section 4.8 of the SmPC to update the ADR table following the assessment of PSUSA (EMEA/H/C/PSUSA/00001467/202112). The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[24]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[25]

7.1.1. Evinacumab - EVKEEZA (CAP) - EMEA/H/C/PSA/S/0098.1

Applicant: Regeneron Ireland DAC

PRAC Rapporteur: Mari Thorn

Scope: Substantial amendment to a protocol for an evaluation of the long-term effects of evinacumab treatment in patients with homozygous familial hypercholesterolemia (HoFH): safety outcomes in patients with HoFH who are ⩾12 years old; frequency and outcomes of pregnancy in female patients with HoFH; atherosclerosis process over time in patients with

[23] Except for centrally authorised product(s)
[24] 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
[25] In accordance with Article 107n of Directive 2001/83/EC

HoFH who undergo cardiovascular imaging (as data allow); frequency of cardiovascular imaging of patients with HoFH

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

7.1.2. Fosdenopterin - NULIBRY (CAP) - EMEA/H/C/PSP/S/0103

Applicant: Zydus France S.A.S.

PRAC Rapporteur: Martin Huber

Scope: Submission of a PASS protocol to characterise and assess the long-term safety and efficacy of NULIBRY prescribed in routine practice for patients with molybdenum cofactor deficiency (MoCD) Type A

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

7.1.3. Valproate[26] (NAP) - EMEA/H/N/PSP/J/0074.6

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Jean-Michel Dogné

Scope: Second interim report: Observational study to evaluate and identify the best practices for switching of valproate in clinical practice

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

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

7.2.1. Avacopan - TAVNEOS (CAP) - EMEA/H/C/005523/MEA 002.2

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002.1 [protocol and feasibility report for study CS-AVA-2022-0016 (listed as category 3 study in the RMP): avacopan real world evidence in anti-neutrophil cytoplasmic autoantibody (ANCA) associated vasculitis - characterisation of the safety concerns of avacopan (i.e. liver injury, serious infections, malignancies and cardiovascular events) beyond the known safety profile based on clinical trial data limited to 52 weeks of exposure] as per request for supplementary information (RSI) adopted in December 2022

Action: For adoption of advice to CHMP

7.2.2. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/MEA 007.1

Applicant: Janssen-Cilag International NV, ATMP[28]

[26] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium
[27] 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
[28] Advanced therapy medicinal product

PRAC Rapporteur: Jo Robays

Scope: 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

Action: For adoption of advice to CAT and CHMP

7.2.3. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 065.2

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of a revised protocol for study mRNA-1273-P910: clinical course, outcomes and risk factors of myocarditis following administration of mRNA-1273 alongside with the second interim report of the study

Action: For adoption of advice to CHMP

7.2.4. Linzagolix choline - YSELTY (CAP) - EMEA/H/C/005442/MEA 002

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of a protocol for study YSELTY PASS: A multinational PASS on real-world treatment in patients receiving YSELTY (linzagolix choline) for moderate to severe symptoms of uterine fibroids, to evaluate routinely collected data on bon mineral density and to assess safety during long term (>12 months) use for linzagolix 200mg (with ABT) and 100mg (with and without ABT) dosing regimen

Action: For adoption of advice to CHMP

7.2.5. Pitolisant - OZAWADE (CAP) - EMEA/H/C/005117/MEA 003

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of a protocol for study P21-02: A multi-center, observational prospective PASS to compare the cardiovascular risks and long-term safety of OZAWADE in patients with obstructive sleep apnoea treated or not by primary therapy and exposed or not to OZAWADE when used in routine medical practice

Action: For adoption of advice to CHMP

7.2.6. Solriamfetol - SUNOSI (CAP) - EMEA/H/C/004893/MEA 002.2

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Julia Pallos

Scope: Submission of a revised protocol (version no.3.0) 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

7.2.7. Tirzepatide - MOUNJARO (CAP) - EMEA/H/C/005620/MEA 002

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a protocol for study I8F-MC-B011: Tirzepatide Pancreatic Malignancy Study to evaluate the incidence of pancreatic malignancy among patients with type 2 diabetes mellitus (T2DM) treated with tirzepatide and to compare the incidence of pancreatic malignancy among patients treated with tirzepatide to patients treated with alternative treatments for clinical indications approved for GLP-1 Ras in Europe

Action: For adoption of advice to CHMP

7.2.8. Tirzepatide - MOUNJARO (CAP) - EMEA/H/C/005620/MEA 005

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a protocol for study I8F-MC-B013: A database linkage study to evaluate the important potential risk of medullary thyroid cancer

Action: For adoption of advice to CHMP

7.2.9. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 062

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

7.3. Results of PASS imposed in the marketing authorisation(s)[29]

None

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[30]

7.4.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0092

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Update of sections 4.6 and 5.3 of the SmPC in order to update information on pregnancy, lactation and fertility following the request by PRAC in the AR for MEA/024.17 and MEA/025.17 and in the PSUR single assessment (PSUSA) procedure (PSUSA/00000086/202109) concluded in June 2022. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

Action: For adoption of PRAC Assessment Report

7.4.2. 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 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

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

7.5.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 006.8

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Semi-annual report for study D8110C00003 (C-VIPER): COVID-19 Vaccines International Pregnancy Registry of Women Exposed to AZD1222 Immediately Before or During Pregnancy (Period covered 01/06/2022-30/11/2022)

Action: For adoption of advice to CHMP

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

7.5.2. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/MEA 003.4

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: 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

Action: For adoption of advice to CHMP

7.5.3. Hydroxycarbamide - SIKLOS (CAP) - EMEA/H/C/000689/MEA 035

Applicant: Addmedica

PRAC Rapporteur: Jo Robays

Scope: Submission of an interim report for study ESCORT-HU Extension: European Sickle Cell Disease Cohort – Hydroxyurea (#2 _V1.0)

Action: For adoption of advice to CHMP

7.5.4. Ketoconazole - KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/ANX 002.10

Applicant: HRA Pharma Rare Diseases

PRAC Rapporteur: Željana Margan Koletić

Scope: MAH's response to ANX 002.9 [Fifth interim annual report for a prospective, multi-country, observational registry study to collect clinical information on patients with endogenous Cushing's syndrome exposed to ketoconazole using the existing European registry on Cushing's syndrome (ERCUSYN) to assess drug utilisation pattern and to document the safety (e.g. hepatotoxicity, QT prolongation) and effectiveness of ketoconazole] as per the request for supplementary information (RSI) adopted in January 2023

Action: For adoption of advice to CHMP

7.5.5. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 004.5

Applicant: Bayer AG

PRAC Rapporteur: Gabriele Maurer

Scope: 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 [final clinical study report (CSR) expected in December 2021]

Action: For adoption of advice to CHMP

7.5.6. Rurioctocog alfa pegol - ADYNOVI (CAP) - EMEA/H/C/004195/ANX 002.2

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study SHP660-403: a PASS to investigate the potential effects of PEG accumulation in the choroid plexus of the brain and other tissues/organs

Action: For adoption of advice to CHMP

7.5.7. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.6

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Fourth interim report for study C4591012: clinical study to assess the occurrence of safety events of interest, including severe or atypical COVID-19 in real-world use of COVID-19 mRNA vaccine

Action: For adoption of advice to CHMP

7.5.8. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.8

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 011.6 [Response to Comirnaty BA.1 and BA.4.5 bivalent vaccine protocol amendments] RSI as adopted in January 2023. Containing a combined justification not to amend the following PASS: C4591010, C4591009, C4591021, and C4591022 regarding Omicron BA.1 and Omicron BA.4-5] as per request for supplementary information (RSI) adopted in December 2022

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/ANX 010.5

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Follow-up from ANX 010.4: The provision of answers to questions about the feasibility report of the non-interventional PASS to investigate drug utilization and safety monitoring patterns for LEMTRADA (Alemtuzumab)

Action: For adoption of advice to CHMP

7.6.2. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 028.4

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH’s response to MEA 028.3 [MAH’s request for cancelling the study PGL18-001: a retrospective drug utilisation study (DUS) through a chart review across four major EU

countries [final study report expected by Q2 2020], as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)] as per the request for supplementary information (RSI) adopted in November 2022

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

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

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Histamine dihydrochloride - CEPLENE (CAP) - EMEA/H/C/000796/S/0045 (without RMP)

Applicant: Laboratoires Delbert

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Tagraxofusp - ELZONRIS (CAP) - EMEA/H/C/005031/S/0020 (without RMP)

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

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

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Bulevirtide - HEPCLUDEX (CAP) - EMEA/H/C/004854/R/0024 (without RMP)

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Entrectinib - ROZLYTREK (CAP) - EMEA/H/C/004936/R/0015 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Idecabtagene vicleucel - ABECMA (CAP) - EMEA/H/C/004662/R/0029 (without RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP[31]

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.5. Imlifidase - IDEFIRIX (CAP) - EMEA/H/C/004849/R/0014 (without RMP)

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

[31] Advanced therapy medicinal product

8.2.6. Pretomanid - DOVPRELA (CAP) - EMEA/H/C/005167/R/0015 (without RMP)

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.7. Valoctocogene roxaparvovec - ROCTAVIAN (CAP) - EMEA/H/C/005830/R/0003 (without RMP)

Applicant: BioMarin International Limited, ATMP[32]

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Abemaciclib - VERZENIOS (CAP) - EMEA/H/C/004302/R/0025 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Binimetinib - MEKTOVI (CAP) - EMEA/H/C/004579/R/0024 (without RMP)

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Buprenorphine - BUVIDAL (CAP) - EMEA/H/C/004651/R/0021 (with RMP)

Applicant: Camurus AB

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

[32] Advanced therapy medicinal product

8.3.4. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/R/0027 (without RMP)

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Deferiprone - DEFERIPRONE LIPOMED (CAP) - EMEA/H/C/004710/R/0011 (with RMP)

Applicant: Lipomed GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Doravirine - PIFELTRO (CAP) - EMEA/H/C/004747/R/0027 (without RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Doravirine, lamivudine, tenofovir disoproxil - DELSTRIGO (CAP) - EMEA/H/C/004746/R/0034 (without RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Encorafenib - BRAFTOVI (CAP) - EMEA/H/C/004580/R/0029 (without RMP)

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Gefitinib - GEFITINIB MYLAN (CAP) - EMEA/H/C/004826/R/0008 (without RMP)

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Pegfilgrastim - PELGRAZ (CAP) - EMEA/H/C/003961/R/0040 (with RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Pegfilgrastim - ZIEXTENZO (CAP) - EMEA/H/C/004802/R/0025 (with RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.14. Vigabatrin - KIGABEQ (CAP) - EMEA/H/C/004534/R/0012 (with RMP)

Applicant: ORPHELIA Pharma SAS

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.15. Vonicog alfa - VEYVONDI (CAP) - EMEA/H/C/004454/R/0027 (with RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. Vote by proxy

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. Marketing authorisation applications (MAA) forecast for 2023 – planning update dated Q1 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

12.13. 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) - publication on EMA website

Action: For discussion

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. Study on the impact of EU label changes for fluoroquinolone-containing medicinal products for systemic and inhalation use: post-referral prescribing trends - follow-up discussion on PRAC Sponsors' assessment

PRAC lead: Eva Jirsová, Martin Huber,

Action: For discussion

12.21. Others

12.21.1. EMA expert management systems update on the new Experts Management Tool

Action: For discussion

12.21.2. Lessons learned on referral procedures – case study

Action: For discussion

12.21.3. PRAC drafting group on the risks of dependence and addiction of opioids - update

Action: For discussion

12.21.4. EMA policy on handling of competing interests for scientific committees' members and experts – revision of policy 0044

Action: For discussion

12.21.5. EFPIA study report on 'Industry perspective on post-authorisation safety study (PASS)' (2016-2022)

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

13. Any other business

Next meeting on: 10-12 May 2023

14. Explanatory notes

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

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

(Items 2 and 3 of the PRAC agenda)

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

Signals assessment and prioritisation

(Item 4 of the PRAC agenda)

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC agenda)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC agenda)

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC agenda)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC agenda)

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

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