04 March 2024
EMA/PRAC/57049/2024
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 04-07 March 2024

Chair: Sabine Straus – Vice-Chair: Martin Huber

04 March 2024, 10:30 – 19:30, via teleconference

05 March 2024, 08:30 – 19:30, via teleconference

06 March 2024, 08:30 – 19:30, via teleconference

07 March 2024, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

21 March 2024, 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 04-07 March 2024. See March 2024 PRAC minutes (to be published post April 2024 PRAC meeting).

1.2. Agenda of the meeting on 04-07 March 2024

Action: For adoption

1.3. Minutes of the previous meeting on 05-08 February 2024

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: various

PRAC Rapporteur: to be appointed

Scope: Signal of pulmonary oedemas

Action: For adoption of PRAC recommendation

EPITT 20050 – New signal

Lead Member State(s): SE

4.1.2. Bumetanide (NAP)

Applicant: various

PRAC Rapporteur: to be appointed

Scope: Signal of toxic epidermal necrolysis

Action: For adoption of PRAC recommendation

EPITT 20033 – New signal

Lead Member State(s): SE

4.1.3. Dupilumab – DUPIXENT (CAP)

Applicant: Sanofi Winthrop Industrie

[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: Kimmo Jaakkola

Scope: Signal of thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 20054 – New signal

Lead Member State(s): FI

4.1.4. Entrectinib – ROZLYTREK (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Signal of myocarditis

Action: For adoption of PRAC recommendation

EPITT 20059 – New signal

Lead Member State(s): NL

4.1.5. Epcoritamab – TEPKINLY (CAP)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Signal of progressive multifocal leukoencephalopathy

Action: For adoption of PRAC recommendation

EPITT 20056 – New signal

Lead Member State(s): ES

4.1.6. Glofitamab – COLUMVI (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Signal of immune effector cell-associated neurotoxicity syndrome

Action: For adoption of PRAC recommendation

EPITT 20058 – New signal

Lead Member State(s): CZ

4.1.7. Human papillomavirus 9-valent vaccine (recombinant, adsorbed) - GARDASIL 9 (CAP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of granuloma

Action: For adoption of PRAC recommendation

EPITT 20046 – New signal

Lead Member State(s): BE

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Abemaciclib – VERZENIOS (CAP) - EMEA/H/C/004302/SDA/004; Palbociclib – IBRANCE (CAP) - EMEA/H/C/003853/SDA/005; Ribociclib – KISQALI (CAP) - EMEA/H/C/004213/SDA/006

Applicant(s): Eli Lilly Nederland B.V. (Verzenios), Pfizer Europe MA EEIG, Novartis Europharm Limited (Kisqali)

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of erythema multiforme

Action: For adoption of PRAC recommendation

EPITT 19973 – Follow-up to October 2023[3]

4.3.2. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/131

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of postmenopausal haemorrhage

Action: For adoption of PRAC recommendation

EPITT 20015 – Follow-up to November 2023[4]

4.3.3. Glucagon-like peptide-1 (GLP-1) receptor agonists: dulaglutide – TRULICITY (CAP) - EMEA/H/C/002825/SDA/015; exenatide – BYDUREON (CAP) - EMEA/H/C/002020/SDA/031, BYETTA (CAP) - EMEA/H/C/000698/SDA/051; insulin degludec, liraglutide – XULTOPHY (CAP) - EMEA/H/C/002647/SDA/003; liraglutide – SAXENDA (CAP) - EMEA/H/C/003780/SDA/021, VICTOZA (CAP) - EMEA/H/C/001026/SDA/041; insulin glargine, lixisenatide – SULIQUA (CAP) - EMEA/H/C/004243/SDA/010; lixisenatide - LYXUMIA (CAP) - EMEA/H/C/002445/SDA/018; semaglutide – OZEMPIC (CAP) - EMEA/H/C/004174/SDA/009, RYBELSUS (CAP) - EMEA/H/C/004953/SDA/014, WEGOVY (CAP) - EMEA/H/C/005422/SDA/008; tirzepatide – MOUNJARO (CAP) - EMEA/H/C/005620/SDA/006

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

[3] Held 25 September – 28 September 2023
[4] Held 23 October – 26 October 2023

Industrie (Lyxumia, Suliqua)

PRAC Rapporteur: Mari Thorn

Scope: Signal of aspiration and pneumonia aspiration

Action: For adoption of PRAC recommendation

EPITT 19974 – Follow-up to October 2023[5]

4.3.4. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/SDA/068

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of postmenopausal haemorrhage

Action: For adoption of PRAC recommendation

EPITT 19989 – Follow-up to November 2023[6]

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. Apadamtase alfa - (CAP MAA) - EMEA/H/C/006198, Orphan

Applicant: Takeda Manufacturing Austria AG

Scope (pre D-180 phase): Treatment of congenital thrombotic thrombocytopenic purpura (cTTP) due to ADAMTS13 deficiency

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

5.1.2. Beremagene geperpavec - (CAP MAA) - EMEA/H/C/006330, PRIME, Orphan

Applicant: Krystal Biotech Netherlands B.V., ATMP

Scope (pre D-120 phase): Treatment of patients from birth with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene

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

[5] Held 25 September – 28 September 2023
[6] Held 23 October – 26 October 2023

5.1.3. Dasatinib - (CAP MAA) - EMEA/H/C/006251

Scope (pre D-180 phase): Treatment of chronic myelogenous leukaemia (CML)

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

5.1.4. Dasiglucagon - (CAP MAA) - EMEA/H/C/006214

Scope (pre D-180 phase): Treatment of severe hypoglycaemia in patients with diabetes

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

5.1.5. Dimethyl fumarate - (CAP MAA) - EMEA/H/C/006471

Scope: Treatment of multiple sclerosis

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

5.1.6. Dimethyl fumarate - (CAP MAA) - EMEA/H/C/006500

Scope: Treatment of multiple sclerosis

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

5.1.7. Fidanacogene elaparvovec - (CAP MAA) - EMEA/H/C/004774, PRIME

ATMP

Scope (pre D-180 phase): 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

5.1.8. RdESAT-6, rCFP-10 - (CAP MAA) - EMEA/H/C/006177

Scope (pre D-180 phase): Diagnosis of infection with *Mycobacterium* tuberculosis

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

5.1.9. Rituximab - (CAP MAA) - EMEA/H/C/006224

Scope (pre D-180 phase): Treatment of non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL) and rheumatoid arthritis

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

5.1.10. Ustekinumab - (CAP MAA) - EMEA/H/C/005918

Scope (pre D-180 phase): Treatment of adult patients with moderately to severely active Crohn’s disease and active ulcerative colitis

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

5.1.11. Zolbetuximab - (CAP MAA) - EMEA/H/C/005868, Orphan

Applicant: Astellas Pharma Europe B.V.

Scope (pre D-180 phase): Treatment of locally advanced unresectable or metastatic HER2 negative gastric or gastro-oesophageal junction (GEJ) adenocarcinoma

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. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/II/0060

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of an updated RMP version 4.2 after approval of adapted COVID-19 vaccine by new strain, Omicron XBB.1.5

Action: For adoption of PRAC Assessment Report

5.2.2. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/II/0091

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Monica Martinez Redondo

Scope: Submission of an updated RMP version 22 in order to include the latest safety information collected until 31 July 2023 (data lock point). The main change consists of removing the neutralising antibodies that cross-react with endogenous thrombopoietin (eTPO)

Action: For adoption of PRAC Assessment Report

5.2.3. Sacituzumab govitecan - TRODELVY (CAP) - EMEA/H/C/005182/II/0031

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Bianca Mulder

Scope: Submission of an updated RMP version 3.1 in order to propose the removal of some safety concerns and the extension of remaining study milestones to date for Category 3 study IMMU-132-15

Action: For adoption of PRAC Assessment Report

5.2.4. Tocofersolan - VEDROP (CAP) - EMEA/H/C/000920/II/0047

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Submission of an updated RMP version 10.1 in order to remove all important

potential risks and missing information from the list of safety concerns, to align with the new RMP format according to Good Pharmacovigilance Practices Module V Revision 2 and to remove one closed PASS of category 2 (Recordati Rare Diseases's Vedrop registry) from the pharmacovigilance plan

Action: For adoption of PRAC Assessment Report

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

5.3.1. Adalimumab - AMGEVITA (CAP) - EMEA/H/C/004212/X/0036/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension application to introduce a new strength, 80 mg [0.8 ml (100 mg/ml)] solution for injection, grouped with various quality variations. :
The RMP (version 6.0) is updated in accordance

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

5.3.2. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/II/0047

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Extension of indication to include the use of Alecensa as monotherapy in adult patients with anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) as adjuvant treatment following tumour resection, based on final results from study BO40336 (ALINA): a randomised, active controlled, multicentre, open-label, Phase III study designed to evaluate the efficacy and safety of alectinib compared with platinum-based chemotherapy in the adjuvant setting in patients with completely resected Stage IB (tumors 4 cm) to Stage IIIA ALKpositive NSCLC. 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 4.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to introduce editorial changes to 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 CHMP

5.3.3. Amivantamab - RYBREVANT (CAP) - EMEA/H/C/005454/II/0011

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include amivantamab in combination with carboplatin and pemetrexed for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) Exon 19 deletions or Exon 21 L858R substitution mutations after failure of prior therapy including a third-generation EGFR tyrosine kinase inhibitor (TKI) for RYBREVANT, based on the final results from study

61186372NSC3002 (MARIPOSA 2); this is a randomised, open label, multicentre Phase 3 study that compares efficacy and safety of amivantamab in combination with carboplatin and pemetrexed (ACP) with carboplatin and pemetrexed (CP). The primary objective of the MARIPOSA 2 study is to compare efficacy, as demonstrated by PFS, in participants treated with ACP versus CP alone. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 6.6 and 9 of the SmPC are updated. The package leaflet is updated in accordance. Version 3.2 of the EU RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) is requesting an additional year of market protection

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

5.3.4. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/II/0044

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information based on the final results from study 18-513 (ANNEXA-I), listed as a specific obligation in the Annex II; this is a phase 4 randomised controlled trial to investigate the efficacy and safety of andexanet alfa versus usual care in patients with acute intracranial haemorrhage taking apixaban, rivaroxaban or edoxaban. Consequently, the MAH proposes a switch from conditional marketing authorisation to full marketing authorisation. The Annex II and package leaflet are updated accordingly. The updated RMP version 4.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information and to bring it 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. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/II/0044/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Monica Martinez Redondo

Scope: A grouped application of a Type II Variation with two Type IA Variations, as follows: Type II (C.I.6.a): Extension of indication to include the treatment of moderate to severe chronic plaque psoriasis in children and adolescents from the age of 6 years who have a contraindication, have an inadequate response, or are intolerant to at least one other systemic therapy or phototherapy for OTEZLA, based on final results from study CC-10004-PPSO-003 as well as results from studies CC-10004-PPSO-001 and CC-10004-PPSO-004. CC-10004-PPSO-003 is a phase 3, multicentre, randomised, double-blind, placebo-controlled study to assess the efficacy and safety of apremilast (CC-10004) in paediatric subjects from 6 through 17 years of age with moderate to severe plaque psoriasis. As a consequence, sections 4.1, 4.2, 4.4 ,4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The package leaflet and labelling are updated in accordance. Version 15.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial and formatting changes to the product information and to update the list of local representatives in the package leaflet.

2 Type IA (B.II.e.5.a.1): Update of sections 6.5 and 8 of the SmPC to introduce two new pack sizes within approved range as a result of the indication update (27 film-coated tablets

(4 x 10 mg, 23 x 20 mg) and 14 film-coated tablets (14 x 20mg), in a pack size of 56 tablets)

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

5.3.6. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/II/0052

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include treatment of eosinophilic granulomatosis with polyangiitis (EGPA) for Fasenra, based on results from study D3253C00001 (Mandara); this was a randomised, double-blind, multicentre, parallel group, active-controlled, non-inferiority study that evaluated the efficacy and safety of benralizumab compared with mepolizumab in treatment of patients with EGPA on corticosteroid therapy with or without stable immunosuppressive therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 6.1 of the RMP has also been submitted. In addition, the MAH took this opportunity to introduce editorial changes. 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

5.3.7. Budesonide, formoterol fumarate dihydrate - BUDESONIDE/FORMOTEROL TEVA PHARMA B.V. (CAP) - EMEA/H/C/004882/II/0012/G

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Grouped variations consisting of: 1) To replace the multidose dry powder inhaler to be used for the delivery of a combination of Budesonide/Formoterol fumarate dihydrate inhalation powder, as well as detect, record, store and transfer inhaler usage information to a mobile application (App); the inhaler is an integrated part of the primary packaging of the medicinal product; 2) To change the name of the medicinal product 3) To update sections 4.2 and 4.4 of the SmPC to reorganise the flow of information within these sections (as approved for DuoResp Spiromax EMEA/H/C/002348), following assessment of the same change for the reference product Symbicort Turbohaler; 4) other quality variations.

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

5.3.8. Cariprazine - REAGILA (CAP) - EMEA/H/C/002770/X/0033

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension application to introduce a new pharmaceutical form (orodispersible tablets). The RMP (version 3.0) is updated in accordance

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

5.3.9. Casirivimab, imdevimab - RONAPREVE (CAP) - EMEA/H/C/005814/II/0015

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.6 of the SmPC in order to update information on pregnancy based on a comprehensive analysis of the results from the drug pregnancy registry cohort (PDC study GV44373), listed as a category 3 PASS in the RMP, as well as data from clinical studies and post-marketing surveillance. The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information 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

5.3.10. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/X/0080/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension application to introduce a new pharmaceutical form (granules in capsules for opening) associated with new strengths (20, 50 and 150 mg), grouped with a type II variation (C.I.6.a) to include the treatment of paediatric patients with relapsed or refractory, systemic ALK-positive ALCL or unresectable, recurrent, or refractory ALK-positive IMT to change the lower end of the age range from ≥6 years to ≥1 year for Xalkori following the assessment of II/0072 based on final results from study ADVL0912. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated in accordance. Version 9.1 of the RMP has also been submitted

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

5.3.11. Dengue tetravalent vaccine[7] (live, attenuated) - DENGUE TETRAVALENT VACCINE (LIVE, ATTENUATED) TAKEDA (Art 58[8]) - EMEA/H/W/005362/WS2593/0012; Dengue tetravalent vaccine (live, attenuated) - QDENGA (CAP) - EMEA/H/C/005155/WS2593/0013

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Update of section 4.5 of the SmPC in order to add co-administration information with HPV vaccine based on final results from study DEN-308 listed as a category 3 study in the RMP (MEA003/MEA004); this is a Phase 3, open-label, randomised trial to investigate the immunogenicity and safety of the co-administration of a subcutaneous dengue tetravalent vaccine (live, attenuated) (TDV) and an intramuscular recombinant 9-valent human papillomavirus (9vHPV) vaccine in subjects aged ≥9 to <15 years in an endemic country for dengue; the package leaflet is updated accordingly. The RMP version 1.1 has

[7] Dengue virus, serotype 2, expressing Dengue virus, serotype 1, surface proteins, live, attenuated, Dengue virus, serotype 2, expressing Dengue virus, serotype 3, surface proteins, live, attenuated, Dengue virus, serotype 2, expressing Dengue virus, serotype 4, surface proteins, live, attenuated, Dengue virus, serotype 2, live, attenuated

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

also been submitted. In addition, the MAH took this opportunity to introduce editorial changes and to update the text on PSUR submissions in Annex II for Dengue tetravalent vaccine

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

5.3.12. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/II/0116

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of paediatric patients from 6 kg to less than 25 kg for Triumeq dispersible tablets, based on PK, safety, and efficacy data observed in the final results of study 205860 (IMPAACT 2019), further supported by extrapolation to data generated in adults and additional data in paediatric patients with the single entities. IMPAACT 2019 is a Phase 1/2 open-label, multicentre, multiple dose study of dolutegravir/lamivudine/abacavir fixed dose combination tablets in treatment-experienced and treatment-naïve HIV-1-infected children less than 12 years of age. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. Version 22.0 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the product information

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

5.3.13. Dolutegravir, rilpivirine - JULUCA (CAP) - EMEA/H/C/004427/II/0057/G

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Nathalie Gault

Scope: Grouped application comprising two type II variations as follows:
C.I.13: Submission of the final report from study 201636 (SWORD 1) listed as a category 3 study in the RMP. This is a phase III, randomised, multicentre, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current INI-, NNRTI-, or product information-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed.
C.I.13: Submission of the final report from study 201637 (SWORD 2) listed as a category 3 study in the RMP. This is a phase III, randomised, multicentre, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current INI-, NNRTI-, or product information-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed. The RMP version 7.0 has also been submitted

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

5.3.14. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0064

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include IMFINZI in combination with platinum-based

chemotherapy as neoadjuvant treatment, followed by IMFINZI as monotherapy after surgery, for the treatment of adults with resectable (tumours ≥ 4 cm and/or node positive) NSCLC and no known EGFR mutations or ALK rearrangements for IMFINZI, based on the interim results from study D9106C00001 (AEGEAN); this is a Phase III, double-blind, placebo-controlled, multicentre international study of neoadjuvant/adjuvant durvalumab for the treatment of patients with resectable stages II and III non-small cell lung cancer. 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 11 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. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/II/0014, Orphan

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of section 4.4 of the SmPC in order to amend an existing warning on infusion reactions and hypersensitivity reactions, and update of section 5.1 of the SmPC to update the mechanism of action of efgartigimod in relation to albumin; based on final results from study ARGX-113-1705 listed a category 3 study in the RMP. This is a long-term, single-arm, open-label, multicentre, phase 3 follow-on study of ARGX-113-1704 to evaluate the safety and tolerability of ARGX-113 in patients with myasthenia gravis having generalised muscle weakness. The RMP version 2.2 has also been submitted

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

5.3.16. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/II/0063

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include treatment of adult men with high-risk biochemical recurrent (BCR) non-metastatic hormone-sensitive prostate cancer (nmHSPC) who are unsuitable for salvage-radiotherapy, for Xtandi, based on final results from study MDV3100-13 (EMBARK); this is a phase 3, randomised, efficacy and safety study of enzalutamide plus leuprolide, enzalutamide monotherapy, and placebo plus leuprolide in men with high-risk non-metastatic prostate cancer progressing after definitive therapy. 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 18.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the product information 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

5.3.17. Faricimab - VABYSMO (CAP) - EMEA/H/C/005642/II/0005

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include treatment of adult patients with visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO) for

Vabysmo, based on results from the two phase 3 studies: GR41984 (BALATON) in patients with branch retinal vein occlusion (BRVO) and GR41986 (COMINO) in patients with central retinal vein occlusion (CRVO) or hemiretinal vein occlusion (HRVO). These are global, multicentre, randomised, double-masked, active comparator-controlled, parallel-group, 2-part studies evaluating the efficacy, safety, and PK of faricimab. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated. The package leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the product information

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

5.3.18. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0022/G, Orphan

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: A grouped application comprised of three Type II variations, as follows:
C.I.4: Update of sections 4.4 and 4.8 of the SmPC in order to modify the list of adverse drug reactions based on a revised safety ADR methodology for Dravet and Lennox-Gastaut syndromes, which includes pooled analyses encompassing studies ZX008-1503 and ZX008-1601 cohort B. The package leaflet is updated accordingly.
C.I.4: Update of section 5.1 of the SmPC in order to update clinical efficacy information for Dravet syndrome based on final results from study ZX008-1503 listed as a category 3 study in the RMP. This is an open-label extension trial to assess the long-term safety of ZX008 (fenfluramine hydrochloride) oral solution as an adjunctive therapy in children and young adults with Dravet syndrome.
C.I.4: Update of section 5.1 of the SmPC in order to update clinical efficacy information for Lennox-Gastaut syndrome based on final results from study ZX008-1601 Part 1 cohort B and interim results for study ZX008-1601 Part 2 cohort B. Study 1601 Part 1 was an international, randomised, double-blind, parallel-group, placebo-controlled study in subjects with LGS 2 to 35 years of age, while study 1601 Part 2 is a long-term, open-label, flexible-dose extension for subjects who completed study 1601 Part 1.
The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the product information, including to section 4.2 of the SmPC

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

5.3.19. Fenofibrate, pravastatin sodium - PRAVAFENIX (CAP) - EMEA/H/C/001243/II/0037

Applicant: Laboratoires SMB s.a.

PRAC Rapporteur: Nathalie Gault

Scope: Extension of indication to include treatment of mixed hyperlipidaemia in adult patients while on a treatment with pravastatin 40 mg monotherapy or on another moderate-intensity statin regimen for PRAVAFENIX, based on final results from the non-interventional PASS: POSE (Pravafenix Observational Study in Europe); this is a European, 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. As a consequence, sections 4.1 and 4.2 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

5.3.20. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/II/0031/G

Applicant: Galapagos N.V.

PRAC Rapporteur: Petar Mas

Scope: Grouped application comprising two variations as follows:

Type II (C.I.4): Update of sections 4.8 and 5.1 of the SmPC to update the safety mean duration exposure and efficacy information based on final results (up to Week 432) from study GLPG0634-CL-205 (DARWIN 3) listed as a category 3 study in the RMP (MEA/009); this is a phase II, open-label, long-term follow-up safety and efficacy study to evaluate the long-term safety and tolerability of filgotinib for the treatment of Rheumatoid Arthritis in patients who received treatment in their parent studies. The RMP version 6.1 has also been submitted.

Type IA (A.6): To change the ATC code for Janus-associated kinase (JAK) inhibitor from L04AA45 filgotinib to L04AF04 filgotinib

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

5.3.21. Ganaxolone - ZTALMY (CAP) - EMEA/H/C/005825/II/0005, Orphan

Applicant: Marinus Pharmaceuticals Emerald Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 4.2 of the SmPC in order to update dosing instructions in severe hepatic impairment based on data from phase I study 1042-IHF-1001. The RMP version 1.3 has also been submitted

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

5.3.22. Imlifidase - IDEFIRIX (CAP) - EMEA/H/C/004849/II/0019, Orphan

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Bianca Mulder

Scope: Update of section 5.1 of the SmPC in order to include the description of the final results from PAES study 17-HMedIdeS-14 listed as a specific obligation in the Annex II (SOB/002); this is a prospective, observational long-term follow-up study of patients treated with imlifidase (IdeS) prior to kidney transplantation. The primary objective of this trial was to evaluate graft survival in patients who have undergone kidney transplantation after imlifidase administration in earlier trials and relates to both safety and efficacy. The RMP version 1.2 has also been submitted. In addition, the MAH took the opportunity to update section E of Annex II and to implement editorial changes to sections 4.4, 4.6 and 9 of the SmPC. Furthermore, 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

5.3.23. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/II/0133/G

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped application comprising three type II variations (C.I.4) as follows:
1) Update of section 4.2, 4.8 and 5.1 of the SmPC in order to add 3-IV induction dosing regimen and dose escalation of subcutaneous maintenance dose from CT-P13 SC 120 mg Q2W to 240 mg Q2W for patients with loss of response and update efficacy and safety information based on Week 54 data from studies CT-P13 3.7 (ulcerative colitis) and CT-P13 3.8 (Crohn's disease), listed as a category 3 study in the RMP; Study CT-P13 3.7 is a randomised, placebo controlled, double-blind, phase 3 study to evaluate the efficacy and safety of the subcutaneous injection of CT-P13 (CT-P13 SC) as maintenance therapy in patients with moderately to severely active ulcerative colitis and study CT-P13 3.8 is a randomised, placebo-controlled, double-blind, phase 3 study to evaluate the efficacy and safety of the subcutaneous injection of CT-P13 (CT-P13 SC) as maintenance therapy in patients with moderately to severely active Crohn's disease.
2) Update of section 4.2 and 5.2 of the SmPC in order to add subcutaneous induction posology and pharmacokinetic information based on Population PK and PK-PD Modelling and Simulation.
3) Update of section 4.2 of the SmPC in order to switch from high-dose IV maintenance (> 5 mg/kg) to subcutaneous maintenance dose of 120 mg every two weeks based on data from REMSWITCH study (Effectiveness of switching from intravenous to subcutaneous infliximab in patients with inflammatory bowel diseases: the REMSWITCH Study).
The RMP version 16.1 has also been submitted. The package leaflet and labelling are updated accordingly. In addition, the MAH took the opportunity to introduce minor updates to the product information

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

5.3.24. Irinotecan hydrochloride trihydrate - ONIVYDE PEGYLATED LIPOSOMAL (CAP) - EMEA/H/C/004125/II/0034, Orphan

Applicant: Les Laboratoires Servier

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include first-line treatment of adult patients with metastatic adenocarcinoma of the pancreas for Onivyde in combination with oxaliplatin, 5 fluorouracil (5 FU) and leucovorin (LV) based on final results from phase 3 study NAPOLI 3 (D-US-60010-001): an interventional study with a primary objective to evaluate the efficacy of the regimen of irinotecan liposome injection + oxaliplatin + 5-fluorouracil (5-FU)/leucovorin (LV) versus nab-paclitaxel + gemcitabine in improving overall survival (OS) in subjects who have not previously received chemotherapy for metastatic adenocarcinoma of the pancreas. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. The updated RMP version 4.1 is also submitted

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

5.3.25. Melatonin - SLENYTO (CAP) - EMEA/H/C/004425/II/0025

Applicant: RAD Neurim Pharmaceuticals EEC SARL

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include treatment of neurogenetic disorders (e.g., Angelman syndrome, Rett syndrome, Tuberous sclerosis complex and Williams syndrome) for SLENYTO, based on Phase III study NEU_CH_7911, post-marketing data and literature; As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.0 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

5.3.26. Mycophenolate mofetil - CELLCEPT (CAP) - EMEA/H/C/000082/II/0170/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Karin Erneholm

Scope: C.I.6.a: Extension of indication to include paediatric patients (3 months to 18 years of age) for hepatic and cardiac transplants and to extend the indication for renal transplants for paediatric patients starting from 3 months, based on pharmacokinetic data, published literature and the Roche Global Safety Database. As a consequence, sections 4.1, 4.2, 4.8 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly. Type IB (C.I.z): To update section 4.2 of the SmPC for the CellCept 500 mg tablets formulation in order to be in line with the other three CellCept formulations. And for alignment with the current QRD guidance, the package leaflet was updated to cross reference section 2 in section 6 for sodium content. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information and 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

5.3.27. Osilodrostat - ISTURISA (CAP) - EMEA/H/C/004821/II/0017/G, Orphan

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped application comprising two type II variations (C.I.4) as follows:
- Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study LINC4 (study CLCI699C2302 - A Phase III, multicenter, randomised, double-blind, 48 week study with an initial 12 week placebo-controlled period to evaluate the safety and efficacy of osilodrostat in patients with Cushing's disease).
- Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study LINC3 (study CLCI699C2301 - A Phase III, multicentre, double-blind, randomised withdrawal study of LCI699 following a 24 week, single-arm, open-label dose titration and treatment period to evaluate the safety and efficacy of LCI699 for the treatment of patients with Cushing's disease).
The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to introduce some minor editorial changes to the

product information

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

5.3.28. Pretomanid - DOVPRELA (CAP) - EMEA/H/C/005167/II/0019/G, Orphan

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Grouped application comprising two variations as follows:
Type II (C.I.4) – Update of sections 4.1 and 5.1 of the SmPC in order to rephrase the indication wording to align with the current WHO definitions. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet.
Type IB (C.I.11.z) - Submission of an updated RMP version 2.0 in order to align the safety concerns following the assessment of procedure EMEA/H/C/005167/11/0013

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

5.3.29. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0053/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Grouped application comprising two extensions of indication to include treatment of paediatric patients weighing at least 1.5 kg for VEKLURY, based on final results from study GS-US-540-5823; this is a Phase 2/3 single-arm, open-label study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of remdesivir in participants from birth to < 18 years of age with COVID-19; 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 8.1 of the RMP has also been submitted

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

5.3.30. Ribociclib - KISQALI (CAP) - EMEA/H/C/004213/II/0045

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Extension of indication to include the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, Stage II or Stage III early breast cancer, irrespective of nodal status, in combination with an aromatase inhibitor (AI) for Kisqali based on study CLEE011O12301C (NATALEE); This is a global, Phase III, multicentre, randomised, open-label trial to evaluate efficacy and safety of ribociclib with endocrine therapy (ET) versus ET alone as adjuvant treatment in patients with HR-positive, HER2-negative, early breast cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated in accordance. Version 8.0 of the RMP 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

5.3.31. Sapropterin - KUVAN (CAP) - EMEA/H/C/000943/II/0078

Applicant: BioMarin International Limited

PRAC Rapporteur: Eamon O'Murchu

Scope: Submission of the final report from study KOGNITO, listed as a category 3 study in the RMP. This is a phase IV open-label, single-cohort study of the long-term neurocognitive outcomes in 4- to 5-year-old children with phenylketonuria treated with sapropterin dihydrochloride (Kuvan) for 7 years. The RMP version 16.0 has also been submitted

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

5.3.32. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/II/0044

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Monica Martinez Redondo

Scope: Extension of indication to include treatment of Polymyalgia Rheumatica (PMR) in adult patients who have had an inadequate response to corticosteroids or who cannot tolerate corticosteroid taper for Kevzara, based on results from study EFC15160; this is a randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of sarilumab in patients with polymyalgia rheumatica; 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 4.0 of the RMP is also 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

5.3.33. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/II/0028

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on interim results from study LIBRETTO-431 (JZJC) listed as a specific obligation in the Annex II (SOB/002); this is a randomised Phase 3 study comparing selpercatinib to platinum-based and pemetrexed therapy with or without pembrolizumab in patients with locally advanced or metastatic, RET-fusion-positive NSCLC. The package leaflet is updated accordingly. The RMP version 6.1 has also been submitted. In addition, the MAH took the opportunity to update Annex II

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

5.3.34. Setmelanotide - IMCIVREE (CAP) - EMEA/H/C/005089/II/0018, Orphan

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Anna Mareková

Scope: Extension of indication to include the population of children aged 2 years and above

for the treatment of pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin Type 1 (PCSK1) deficiency or biallelic leptin receptor (LEPR) deficiency and Bardet-Biedl Syndrome (BBS) for IMCIVREE, based on the final results from study RM-493-033 "A Phase 3 multicentre, one-year, open-label study of setmelanotide in paediatric patients aged 2 to <6 years of age with rare genetic causes of obesity"; this is an open label study to evaluate the weight-related parameters along with the safety and tolerability of setmelanotide in patients aged 2 to <6 years. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. In addition, the MAH took this opportunity to introduce editorial changes to the product information

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

5.3.35. Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara) - IMVANEX (CAP) - EMEA/H/C/002596/II/0100

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Update of section 5.1 of the SmPC in order to add vaccine effectiveness data, and the removal of the two open specific obligations (POX-MVA-039 (SOB02) and SEMVAc (SOB03)), based on the IMVANEX vaccine effectiveness data in real-world use during the 2022 monkeypox outbreak. Consequently, the MAH proposes a switch from exceptional marketing authorisation to full marketing authorisation. 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

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

5.3.36. Spesolimab - SPEVIGO (CAP) - EMEA/H/C/005874/X/0006/G

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nathalie Gault

Scope: Extension application to introduce a new pharmaceutical form (solution for injection) associated with a new strength (150 mg) and new route of administration (subcutaneous use), for the prevention of generalised pustular psoriasis (GPP) flares in adults and adolescents from 12 years of age. This line extension is grouped with a type II variation (C.I.6.a) to extend indication for Spevigo 450 mg concentrate for solution for infusion to include treatment of generalised pustular psoriasis (GPP) flares in adolescents (from 12 years of age), based on final results from study 1368-0027 (Effisayil 2) and extrapolation; this is a multi-centre, randomised, parallel group, double blind, placebo controlled, phase IIb dose-finding study to evaluate efficacy and safety of BI 655130 (spesolimab) compared to placebo in preventing GPP flares in patients with history of GPP. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Annex II and package leaflet are updated in accordance. Version 2.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce 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

5.3.37. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/II/0054

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 5.1 of the SmPC in order to update clinical and safety information based on long-term results from the extension periods of the pivotal clinical studies MK-3222-010 (A 64-Week, Phase 3, Randomised, Placebo-Controlled, Parallel Design Study to Evaluate the Efficacy and Safety/Tolerability of Subcutaneous Tildrakizumab (SCH 900222/MK-3222), Followed by an Optional Long-Term Safety Extension Study, in Subjects with Moderate-to-Severe Chronic Plaque Psoriasis (Protocol No. MK-3222-010)) and MK-3222-011 (A 52-Week, Phase 3, Randomised, Active Comparator and Placebo-Controlled, Parallel Design Study to Evaluate the Efficacy and Safety/Tolerability of Subcutaneous Tildrakizumab (SCH 900222 / MK-3222), Followed by an Optional Long-Term Safety Extension Study, in Subjects With Moderate-to-Severe Chronic Plaque Psoriasis). The RMP version 1.4 has also been submitted

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

5.3.38. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0121

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final report from study ZUMA-8 (PAM). This is a phase 1 multicenter study evaluating the safety and tolerability of KTE-X19 in adult subjects with Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma. The RMP version 29.0 has also been submitted

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

5.3.39. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/II/0201

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Update of sections 4.5, 4.8 and 5.1 of the SmPC in order to update information regarding concomitant vaccine administration with influenza vaccine based on final results from study C4591030 listed as a category 3 study in the RMP. This is an interventional phase 3, randomised, observer-blind trial to evaluate the safety and immunogenicity of BNT162b2 and quadrivalent seasonal influenza vaccine when administered separately or concomitantly in adults 18 to 64 years of age. The package leaflet is updated accordingly. The RMP version 11.1 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. Anifrolumab - SAPHNELO (CAP) - PSUSA/00010980/202307

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Ataluren - TRANSLARNA[9] (CAP) - PSUSA/00010274/202307

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Avalglucosidase alfa - NEXVIADYME (CAP) - PSUSA/00011002/202308

Applicant: Sanofi B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Belantamab mafodotin - BLENREP (CAP) - PSUSA/00010869/202308

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Bimekizumab - BIMZELX (CAP) - PSUSA/00010953/202308

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

[9] EMA confirms recommendation for non-renewal of authorisation of Duchenne muscular dystrophy medicine Translarna | European Medicines Agency (europa.eu)

Action: For adoption of recommendation to CHMP

6.1.6. Bulevirtide - HEPCLUDEX (CAP) - PSUSA/00010873/202307

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Catridecacog - NOVOTHIRTEEN (CAP) - PSUSA/00010034/202307

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Corifollitropin alfa - ELONVA (CAP) - PSUSA/00000875/202307

Applicant: Organon N.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Darolutamide - NUBEQA (CAP) - PSUSA/00010843/202307

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Dengue tetravalent vaccine (live, attenuated) - DENGUE TETRAVALENT VACCINE (Art 58[10]) - EMEA/H/W/005362/PSUV/0011

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

[10] 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)

6.1.11. Dengue tetravalent vaccine[11] (live, attenuated) - QDENGA (CAP) - PSUSA/00011034/202308

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Difelikefalin - KAPRUVIA (CAP) - PSUSA/00010995/202308

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Eptinezumab - VYEPTI (CAP) - PSUSA/00010966/202308

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Evinacumab - EVKEEZA (CAP) - PSUSA/00010945/202308

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Evolocumab - REPATHA (CAP) - PSUSA/00010405/202307

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[11] Dengue virus, serotype 2, expressing Dengue virus, serotype 1, surface proteins, live, attenuated, Dengue virus, serotype 2, expressing Dengue virus, serotype 3, surface proteins, live, attenuated, Dengue virus, serotype 2, expressing Dengue virus, serotype 4, surface proteins, live, attenuated, Dengue virus, serotype 2, live, attenuated

6.1.16. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/202308

Applicant: Holostem S.r.l., ATMP

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.17. Fedratinib - INREBIC (CAP) - PSUSA/00010909/202308

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Hydrocortisone[12] - ALKINDI (CAP) - PSUSA/00010674/202308

Applicant: Diurnal Europe BV

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Ibuprofen[13] - PEDEA (CAP) - PSUSA/00001712/202307

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Lanadelumab - TAKHZYRO (CAP) - PSUSA/00010743/202308

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Lefamulin - XENLETA (CAP) - PSUSA/00010872/202308

Applicant: Nabriva Therapeutics Ireland DAC

[12] Centrally authorised products indicated for treatment of adrenal insufficiency, paediatric use only
[13] Indicated in ductus arteriosus

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Lenacapavir - SUNLENCA (CAP) - PSUSA/00011012/202308

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Lisocabtagene maraleucel, lisocabtagene maraleucel - BREYANZI (CAP) - PSUSA/00010990/202308

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

6.1.24. Lomitapide - LOJUXTA (CAP) - PSUSA/00010112/202307

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Melphalan flufenamide - PEPAXTI (CAP) - PSUSA/00011013/202308

Applicant: Oncopeptides AB

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Methoxy polyethylene glycol-epoetin beta - MIRCERA (CAP) - PSUSA/00002017/202307

Applicant: Roche Registration GmbH

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Mitapivat - PYRUKYND (CAP) - PSUSA/00011025/202308

Applicant: Agios Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Palbociclib - IBRANCE (CAP) - PSUSA/00010544/202308

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Panobinostat - FARYDAK (CAP) - PSUSA/00010409/202308

Applicant: Pharmaand GmbH

PRAC Rapporteur: Sofia Trantza

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Patisiran - ONPATTRO (CAP) - PSUSA/00010715/202308

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Pretomanid - DOVPRELA (CAP) - PSUSA/00010863/202308

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Regdanvimab - REGKIRONA (CAP) - PSUSA/00010964/202308

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Risdiplam - EVRYSDI (CAP) - PSUSA/00010925/202308

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Sacubitril, valsartan - ENTRESTO (CAP); NEPARVIS (CAP) - PSUSA/00010438/202307

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Saxagliptin – ONGLYZA (CAP); saxagliptin, metformin - KOMBOGLYZE (CAP) - PSUSA/00002685/202307

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara) - IMVANEX (CAP) - PSUSA/00010119/202307

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Sotrovimab - XEVUDY (CAP) - PSUSA/00010973/202308

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Sutimlimab - ENJAYMO (CAP) - PSUSA/00011023/202308

Applicant: Sanofi B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Tafasitamab - MINJUVI (CAP) - PSUSA/00010951/202307

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Teclistamab - TECVAYLI (CAP) - PSUSA/00011010/202308

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Temozolomide - TEMODAL (CAP) - PSUSA/00002886/202307

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Tisagenlecleucel - KYMRIAH (CAP) - PSUSA/00010702/202308

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.43. Tocofersolan - VEDROP (CAP) - PSUSA/00002981/202307

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Upadacitinib - RINVOQ (CAP) - PSUSA/00010823/202308

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Voxelotor - OXBRYTA (CAP) - PSUSA/00010983/202308

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Jo Robays

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. Aripiprazole - ABILIFY (CAP); ABILIFY MAINTENA (CAP); ARIPIPRAZOLE SANDOZ (CAP); NAP - PSUSA/00000234/202307

Applicant: Otsuka Pharmaceutical Netherlands B.V. (Abilify, Abilify Maintena), Sandoz GmbH (Aripiprazole Sandoz), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Eflornithine[14] - VANIQA (CAP); NAP - PSUSA/00001202/202307

Applicant: Almirall S.A (Vaniqa), various

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Leuprorelin[15] - CAMCEVI (CAP); NAP - PSUSA/00010877/202307

Applicant: Accord Healthcare S.L.U. (Camcevi), various

[14] Topical use only
[15] Depot formulation(s) only

PRAC Rapporteur: Amelia Cupelli

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. Aciclovir, hydrocortisone (NAP) - PSUSA/00009004/202307

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Anastrozole (NAP) - PSUSA/00000210/202308

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Atorvastatin, ezetimibe (NAP) – PSUSA/00010385/202307

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Colchicine (NAP) - PSUSA/00000858/202307

Applicant(s): various

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Donepezil, memantine (NAP) - PSUSA/00011039/202307

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Ezetimibe, rosuvastatin (NAP) - PSUSA/00010271/202307

Applicant(s): various

PRAC Lead: Barbara Kovačić Bytyqi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Fenofibrate (NAP) - PSUSA/00001362/202307

Applicant(s): various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Indometacin (NAP) - PSUSA/00001738/202307

Applicant(s): various

PRAC Lead: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Inosine pranobex (NAP) - PSUSA/00010425/202308

Applicant(s): various

PRAC Lead: Irina Sandu

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Niclosamide (NAP) - PSUSA/00002151/202308

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Paracetamol, tramadol (NAP) - PSUSA/00002310/202308

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Ribavirin[16] (NAP)[17] - PSUSA/00010007/202307

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Quetiapine (NAP) - PSUSA/00002589/202307

Applicant(s): various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/LEG 008

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of a safety review on cases craniosynostosis as per the conclusions from PSUSA/00010669/202302 adopted by PRAC in October 2023.

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/II/0254

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Update of section 4.8 of the SmPC in order to update the frequency of Adverse Drug Reaction (ADR) 'glomerulonephritis' from 'not known' to 'rare' following PSUSA/00010795/202302 procedure, based on available evidence from clinical trials, literature, and post-marketing data. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

[16] Oral formulation(s) only
[17] Ribavirin - REBETOL (CAP) - European Commission (EC) decision on the withdrawal of the marketing authorisation (MA) dated 18 October 2023

6.5.2. Isatuximab - SARCLISA (CAP) - EMEA/H/C/004977/II/0027

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Monica Martinez Redondo

Scope: Update of section 4.8 of the SmPC in order to add 'thrombocytopenia' and 'anaemia' to the list of adverse drug reactions (ADRs) and to amend the frequency of all remaining ADRs with their appropriate frequencies, following PRAC request in the outcome of the PSUSA procedure PSUSA/00010851/202303

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[18]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[19]

7.1.1. Blinatumomab - Blincyto (CAP) - EMEA/H/C/PSA/S/0111

Applicant: Sanofi Belgium

PRAC Rapporteur: Jana Lukacisinova

Scope: Substantial amendment to a protocol for an observational study of blinatumomab safety and effectiveness, utilisation, and treatment practices

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

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

7.2.1. Avatrombopag - DOPTELET (CAP) - EMEA/H/C/004722/MEA 002.7

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Monica Martinez Redondo

Scope: MAH's response to MEA 002.6 [Revised Protocol / Study Number: AVA-CLD-402] as per RSI as adopted in October 2023

Action: For adoption of advice to CHMP

[18] 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
[19] In accordance with Article 107n of Directive 2001/83/EC
[20] 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. Cabotegravir - APRETUDE (CAP) - EMEA/H/C/005756/MEA 003

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Protocol for study CAB LA PrEP Cohort: Prospective Cohort Study to Assess Adherence and Effectiveness of, and Monitor for Hepatotoxicity and Resistance to Cabotegravir for Pre-Exposure Prophylaxis in Europe

Action: For adoption of advice to CHMP

7.2.3. Cannabidiol - EPIDYOLEX (CAP) - EMEA/H/C/004675/MEA 007.4

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Revised Protocol v. for study GWEP19022 (listed as a category 3 study in the RMP): a prospective, observational cohort long-term safety study to assess the potential for chronic liver injury in patients treated with Epidyolex (cannabidiol oral solution) when used under conditions of routine clinical care as per the request for supplementary information (RSI) adopted in November 2023

Action: For adoption of advice to CHMP

7.2.4. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/MEA 092.5

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Amended PASS protocol / Study number: 20190404; Title: Use of Erythropoiesis Stimulating Agents (ESAs) in Subjects Receiving Myelosuppressive Chemotherapy in Europe

Action: For adoption of advice to CHMP

7.2.5. Eptinezumab - VYEPTI (CAP) - EMEA/H/C/005287/MEA 004.4

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Martirosyan

Scope: MAH’s response to MEA 004.3 [Revised Protocol - Master Study No. 19756N; Observational, historical cohort study of patients initiating eptinezumab in routine clinical practice and is investigating the long-term cardiovascular safety and real-world use of Eptinezumab] as per the request for supplementary information (RSI) adopted in October 2023

Action: For adoption of advice to CHMP

7.2.6. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 001.9

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

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

Action: For adoption of advice to CHMP

7.2.7. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/MEA 001.4

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: From Initial MAA: REVISED PROTOCOL 0.3 FOR PASS EUPAS31436
To Characterise the Safety of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) in Patients with Cutaneous T-Cell Lymphoma (CTCL) treated with Mogamulizumab

Action: For adoption of advice to CHMP

7.2.8. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/MEA 002.5

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Early study termination proposal with the original justification document - Clinical Study Protocol PASS 3000-04-001 Version 8
Draft protocol amendment for EUPAS 29407 (in track changes) incorporating the changes related to the early termination proposal:
- New proposed end of data collection (data cut-off date): Q2 2024 (current date: Q3 2026)
- New proposed final report submission: Q4 2024 (current date: Q1 2027)
- Removal of the exploratory objective and related information

Action: For adoption of advice to CHMP

7.2.9. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 001.3

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the Ozanimod Real World Safety:
A Post Authorisation Multi National Long term Non Interventional Study (ORION) study (Categ. 3) protocol for approval within 6 months after the marketing authorisation for Zeposia is granted.
***Revised protocol / IM047-009 (ORION) version 5.0 ***

[future due date(s):
Interim study results: 31 Dec. 2025
Final CSR: 31 Dec. 2031]

Action: For adoption of advice to CHMP

7.2.10. Voclosporin - LUPKYNIS (CAP) - EMEA/H/C/005256/MEA 002.2

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 002.1 [PASS Protocol No 348-201-00021] as adopted in November 2023. Observational PASS in Europe to further characterise and quantify long-term safety profile with respect to neurotoxicity, chronic nephrotoxicity, and malignancy with use of voclosporin (category 3 study in the RMP)

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[21]

7.3.1. Aclidinium - BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP); aclidinium, formoterol fumarate dihydrate – BRIMICA GENUAIR (CAP), DUAKLIR GENUAIR (CAP) - EMEA/H/C/PSR/S/0047

Applicant: Covis Pharma Europe B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Final study report for a PASS to evaluate the potential cardiovascular safety concerns and all-cause mortality described in the risk management plan for aclidinium bromide as monotherapy and fixed-dose combination of aclidinium/formoterol

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[22]

7.4.1. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/II/0033/G

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final reports from the Drug Utilisation Study of Intuniv (guanfacine extended release) in European countries: a prescriber survey (EUPAS18739) and a retrospective database study (EUPAS18735), listed as category 3 studies in the RMP. The RMP version 4.0 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.2. Human normal immunoglobulin - HYQVIA (CAP) - EMEA/H/C/002491/II/0096

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Gabriele Maurer

[21] In accordance with Article 107p-q of Directive 2001/83/EC
[22] 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

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update long-term safety information based on final results from studies 161406 "Non-Interventional Post-Marketing Safety Study on the Long-Term Safety of HYQVIA (Global)" listed as category 3 a study in the RMP and 161302 "Non-Interventional PASS on the Long-Term Safety of HyQvia in Subjects Treated with HyQvia". Both studies were non-interventional, prospective, uncontrolled, multicenter, open-label, post-authorisation studies. The RMP version 15.0 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, to update the list of local representatives in the package leaflet and to introduce minor editorial changes to the product information

Action: For adoption of PRAC Assessment Report

7.4.3. Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/II/0081

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 4.6 of the SmPC in order to update information on pregnancy based on final results from study Vedolizumab-5001 (OTIS Entyvio Pregnancy Exposure Registry); this is a non-interventional study to monitor planned and unplanned pregnancies in female patients with ulcerative colitis or Crohn's disease. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor changes and corrections to the product information and bring it in line with the latest QRD template

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 021.1

Applicant: Bayer AG

PRAC Rapporteur: Nathalie Gault

Scope: From II-0068 and II-0075 (RMP); Second Annual Safety Report; Intraocular Pressure Increase with the Eylea PFS

Action: For adoption of advice to CHMP

7.5.2. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.16

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: From initial MAA; Ninth Annual Progress Report, Study (PASS) OBS13434 (non-imposed/non-interventional); This annual progress report covers the period from 01-Jan-2023 to 06-Oct-2023. A progress report will be compiled on an annual basis in order to meet applicable regulatory commitments. Study data for patient demographics and baseline disposition as well as an overview of all adverse events including AESIs and serious adverse

events is no longer included in the annual PASS progress report as agreed with the procedure manager at time of previous PASS annual progress report 3

Action: For adoption of advice to CHMP

7.5.3. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/ANX 009.5

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: PASS Mortality Interim Study Result / CSA0002; REAL WORLD AND EPIDEMIOLOGY STUDY REPORT; A non-interventional PASS to investigate the risk of mortality in multiple sclerosis patients treated with alemtuzumab (LEMTRADA) relative to comparable multiple sclerosis patients using other disease modifying therapies: A cohort study

Action: For adoption of advice to CHMP

7.5.4. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/SOB 009.2

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: MAH's responses to SOB009.1 [Study BLU-285-1406 is a multinational, open-label, observational PASS that will evaluate the long-term safety and efficacy of avapritinib for the first-line treatment or following ≤4 months of imatinib treatment in at least 50 patients with PDGFRA D842V-mutated GIST.] RSI as adopted in November 2023

Action: For adoption of advice to CHMP

7.5.5. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 004.7

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Third interim report for study D3250R00042: a descriptive study of the incidence of malignancy in patients with severe asthma overall and among those receiving benralizumab and other therapies in real-world settings

Action: For adoption of advice to CHMP

7.5.6. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 005.1

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: MAH's response to questions on MEA 005 [Study PS0014] as adopted in November 2023

Action: For adoption of advice to CHMP

7.5.7. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 004.5

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: MAH's response to MEA 004.4 [Protocol, study no. 2019nCoV-402] as per RSI as adopted in October 2023

Action: For adoption of advice to CHMP

7.5.8. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 009.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: 4th interim report of study MB102118: Pharmacoepidemiology study assessing the risk of cancer. Evaluate cancer (Study MB102-118ST/D1690R00007 - (EUPAS12116))

Action: For adoption of advice to CHMP

7.5.9. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/MEA 004.9

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: 4th interim report of study MB102118: Pharmacoepidemiology study assessing the risk of cancer. Evaluate cancer (Study MB102-118ST/D1690R00007 -(EUPAS12116))

Action: For adoption of advice to CHMP

7.5.10. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/ANX 038.15

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Tenth Annual Interim Safety Report for Study CICL670E2422; An observational, multi-center study to evaluate the safety of deferasirox in the treatment of pediatric patients with non-transfusion-dependent iron overload

Action: For adoption of advice to CHMP

7.5.11. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/MEA 062.2

Applicant: Alexion Europe SAS

PRAC Rapporteur: Monica Martinez Redondo

Scope: aHUS Registry Biennial Interim Report /Protocol M11-001; Title: An Observational, non-interventional multicenter, multinational study of patients with atypical hemolytic-uremic syndrome

Action: For adoption of advice to CHMP

7.5.12. Esketamine - SPRAVATO (CAP) - EMEA/H/C/004535/MEA 003.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Interim Study /Study no.: PCSNSP002812; Survey to Assess the Effectiveness of SPRAVATO Educational Materials for Additional Risk Minimization Measures in the European Union

Action: For adoption of advice to CHMP

7.5.13. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 038.7

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: FOURTH interim report of the open-label extension phase of study CFTY720D2311 to collect long term safety data (RMP Category 3 study). Study CFTY720D2311: A two-year, double-blind, randomised, multicenter, active-controlled Core Phase study to evaluate the safety and efficacy of fingolimod administered orally once daily versus interferon β-1a i.m. once weekly in pediatric patients with multiple sclerosis with five-year fingolimod Extension Phase

Action: For adoption of advice to CHMP

7.5.14. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 003.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: From Initial MAA: Galcanezumab European Drug Utilization and Safety Outcomes Study (Planned).
- To describe, in real-world clinical practice, the utilization of galcanezumab in Europe, and the incidence of important safety outcomes such as serious hypersensitivity and long-term safety including serious cardio-vascular events, and malignancies.
- The secondary objective is to provide context for incidence rates of safety events seen in the galcanezumab cohort by describing the incidence rates observed in a comparator cohort and, as feasible, to conduct comparative safety analyses of serious cardiovascular events, serious hypersensitivity reactions, and malignancies using patients initiated on other prophylactic migraine medication as a control. (Cat. 3)

Action: For adoption of advice to CHMP

7.5.15. Human C1-esterase inhibitor - CINRYZE (CAP) - EMEA/H/C/001207/MEA 021.1

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Gabriele Maurer

Scope: IOS interim Clinical Study Report; Encompassing data of 199 Cinryze-treated patients. Additionally, at least 45 unique SHP616-401

Action: For adoption of advice to CHMP

7.5.16. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/MEA 002.6

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Third Annual Interim Study Report / VX20-445-120; Title: Real-World Effects and Utilisation Patterns of Elexacaftor, Tezacaftor, and Ivacaftor Combination Therapy (ELX/TEZ/IVA) in Patients with Cystic Fibrosis (CF)

Action: For adoption of advice to CHMP

7.5.17. Naldemedine - RIZMOIC (CAP) - EMEA/H/C/004256/MEA 001.7

Applicant: Shionogi B.V.

PRAC Rapporteur: Eamon O'Murchu

Scope: 2nd Annual Progress Report with interim report of study results for An Observational PASS of Patients with Chronic Opioid Use for Non-Cancer and Cancer Pain who have Opioid-Induced Constipation (OIC)

Action: For adoption of advice to CHMP

7.5.18. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/ANX 001

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: From initial MAA: Fifth Progress Report (yearly) and Second Interim Report for PASS NN7999-4031/Paradigm 8: A Non-Interventional PASS in male haemophilia B patients receiving Nonacog Beta Pegol

Action: For adoption of advice to CHMP

7.5.19. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 002.4

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: SECOND INTERIM REPORT for PASS Study COMB157G2407 (cat. 3): Evaluation of pregnancy and infant outcomes in Kesimpta patients using PRegnancy outcomes Intensive Monitoring (PRIM) data – The Kesimpta-PRIM study

Action: For adoption of advice to CHMP

7.5.20. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 003.6

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: SECOND INTERIM REPORT for Study 165-501; A prospective, global observational exposure study. Title: A Multi-Center, Observational Study to Evaluate the Long Term

Safety of Subcutaneous Injections of Pegvaliase in Patients with Phenylketonuria

Action: For adoption of advice to CHMP

7.5.21. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 005.8

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Second Interim Report / study number: 165-504; Title: A global multicentre study to assess maternal, fetal and infant outcomes of exposure to Palynziq (pegvaliase) during pregnancy and breastfeeding

Action: For adoption of advice to CHMP

7.5.22. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[23]) - EMEA/H/W/002300/MEA 003.9

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Ninth Progress Report for Study EPI-MAL-003: Estimate the incidence of protocol-defined potential adverse events of special interest (AESI) and other adverse events leading to hospitalisation or death, in children vaccinated with RTS,S/AS01E enrolled during the EPI-MAL-003 study

Action: For adoption of advice to CHMP

7.5.23. Sebelipase alfa - KANUMA (CAP) - EMEA/H/C/004004/ANX 001.6

Applicant: Alexion Europe SAS

PRAC Rapporteur: Mari Thorn

Scope: From Initial MAA: Non-interventional PASS: LAL Deficiency Registry: Non-interventional, multicentre, prospective disease and clinical outcome registry of patients with Lysosomal Acid Lipase Deficiency to further understand the disease, its progression and any associated complication, and to evaluate the long-term efficacy (normalisation of hepatic function) and safety of Kanuma (in particular hypersensitivity reactions, including anaphylaxis, and anti-drug antibodies development potentially impacting response to drug) according to agreed protocol

Action: For adoption of advice to CHMP

7.5.24. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.8

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: FOURTH Annual Interim Results/ Study No.: M-14745-40; Title: Tildrakizumab PASS

[23] 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)

in European Psoriasis Registries

Action: For adoption of advice to CHMP

7.5.25. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 041.5

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Third Interim Report / Study C4591036; Clinical study to characterize the clinical course, risk factors, long-term sequelae, and quality of life in children and young adults <21 years with acute post-vaccine myocarditis

Action: For adoption of advice to CHMP

7.5.26. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/MEA 029

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Martin Huber

Scope: Annual Report for the Gaucher Outcome Survey (GOS) 2023; Title: Gaucher Disease Outcome Survey (GOS) An Observational, International, Multi-center, Long-term Registry of Patients with Gaucher Disease

Action: For adoption of advice to CHMP

7.5.27. Vosoritide - VOXZOGO (CAP) - EMEA/H/C/005475/MEA 005.4

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: First Biannual Report / BMN111-603 (period from 17 Apr 2023 to 25 Aug 2023); A multicenter, non-interventional study to evaluate long-term safety in patients with achondroplasia treated with Voxzogo (vosoritide)

Action: For adoption of advice to CHMP

7.6. Others

None

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/S/0064 (without RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Mari Thorn

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. Entrectinib - ROZLYTREK (CAP) - EMEA/H/C/004936/R/0020 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Futibatinib - LYTGOBI (CAP) - EMEA/H/C/005627/R/0003 (without RMP)

Applicant: Taiho Pharma Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Glofitamab - COLUMVI (CAP) - EMEA/H/C/005751/R/0003 (with RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Angiotensin II - GIAPREZA (CAP) - EMEA/H/C/004930/R/0027 (without RMP)

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Botulinum toxin type A - NUCEIVA (CAP) - EMEA/H/C/004587/R/0037 (without RMP)

Applicant: Evolus Pharma B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Deferasirox - DEFERASIROX MYLAN (CAP) - EMEA/H/C/005014/R/0013 (without RMP)

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Trientine - CUFENCE (CAP) - EMEA/H/C/004111/R/0016 (without RMP)

Applicant: Univar Solutions BV

PRAC Rapporteur: Ana Sofia Diniz Martins

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

11.2.1. Cardioplexol (NAP)

PRAC Lead: Jan Neuhauser

Scope: PRAC consultation on the evaluation of an initial marketing authorisation application under the decentralised procedure for cardioplexol in order to consider the need for additional pharmacovigilance activities and risk minimisation measures, on request of

Austria

Action: For adoption of advice to Member States

11.2.2. Valproate[24] (NAP) - NL/H/xxxx/WS/794

Applicant(s): Sanofi-Aventis Recherche & Développement (on behalf of a consortium)

PRAC Lead: Liana Martirosyan

Scope: PRAC consultation on a work sharing variation, with focus on the assessment of the protocol of the qualitative study proposed by the Consortium of MAHs (cat.1 PASS to provide the results of the additional analyses requested in the framework of the assessment of the results of study EUPAS34201 on paternal exposure to valproate) following PRAC recommendation on valproate-containing medicinal products (see PRAC minutes January 2024), on request of the Netherlands

Action: For adoption of advice to Member States

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. Health threats and EMA Emergency Task Force (ETF) activities - update

Action: For discussion

[24] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpromide, valproate bismuth, calcium valproate, valproate magnesium

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Jana Lukačišinová

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: Martin Huber

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

12.13.2. Eudravigilance annual report 2023

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

12.20.1. GVP Module XVI (Rev.3) on Risk Minimisation Measures: post-public consultation draft Addendum II on Methods for Effectiveness Evaluation

PRAC lead: Liana Martirosyan

Action: For discussion

12.20.2. Joint Heads of Medicines Agencies (HMA)/European Medicines Agency (EMA) Multistakeholder workshop on Patient Registries

Action: For discussion

12.21. Others

12.21.1. Amendments to the Commission Implementing Regulation (EU) No 520/2012 on the performance of pharmacovigilance activities - update

Action: For discussion

13. Any other business

Next meeting on: 08-11 April 2024

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

Pharmacovigilance Risk Assessment Committee (PRAC)

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