10 May 2023
EMA/PRAC/213551/2023
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 10-12 May 2023

Chair: Sabine Straus – Vice-Chair: Martin Huber

10 May 2023, 08:30 – 19:30, via teleconference

11 May 2023, 08:30 – 19:30, via teleconference

12 May 2023, 08:30 – 19:30, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

23 May 2023, 09:00 – 12:00, via teleconference

Disclaimers

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

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

Note on access to documents

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

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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 10-12 May 2023. See May 2023 PRAC minutes (to be published post June 2023 PRAC meeting).

1.2. Agenda of the meeting on 10-12 May 2023

Action: For adoption

1.3. Minutes of the previous meeting on 11-14 April 2023

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

3.1.1. Hydroxyprogesterone (NAP) - EMEA/H/A-31/1528

Applicant(s): various

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

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

Action: For adoption of a list of questions

3.2. Ongoing procedures

3.2.1. Pseudoephedrine (NAP); pseudoephedrine, acetylsalicylic acid (NAP); pseudoephedrine, acetylcysteine, paracetamol (NAP); pseudoephedrine, acrivastine (NAP); pseudoephedrine, ascorbic acid, paracetamol (NAP); pseudoephedrine, cetirizine (NAP); pseudoephedrine, ebastine (NAP); pseudoephedrine, guaifenesin (NAP); pseudoephedrine, ibuprofen (NAP); pseudoephedrine, chlorphenamine (NAP); pseudoephedrine, chlorphenamine, codeine (NAP); pseudoephedrine, chlorphenamine, dextromethorphan (NAP); pseudoephedrine, chlorphenamine, paracetamol (NAP); pseudoephedrine, chlorphenamine, dextromethorphan, paracetamol (NAP); pseudoephedrine, dextromethorphan (NAP); pseudoephedrine, dextromethorphan, paracetamol (NAP); pseudoephedrine, dextromethorphan, ascorbic acid, paracetamol (NAP); pseudoephedrine, dextromethorphan, guaifenesin, paracetamol (NAP); pseudoephedrine, dextromethorphan, guaifenesin, triprolidine (NAP); pseudoephedrine, dextromethorphan, triprolidine (NAP); pseudoephedrine, diphenhydramine, paracetamol (NAP); pseudoephedrine, doxylamine, paracetamol (NAP); pseudoephedrine, loratadine (NAP); pseudoephedrine, paracetamol (NAP); pseudoephedrine, paracetamol, pholcodine (NAP); pseudoephedrine, triprolidine (NAP); pseudoephedrine, triprolidine, guaifenesin (NAP); pseudoephedrine, triprolidine, paracetamol (NAP); pseudoephedrine, desloratadine - AERINAZE (CAP) – EMA/H/A-31/1526

Applicant(s): various

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

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

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

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

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

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Azacitidine – AZACITIDINE ACCORD (CAP), AZACITIDINE BETAPHARM (CAP), AZACITIDINE MYLAN (CAP), ONUREG (CAP), VIDAZA (CAP)

Applicant(s): Accord Healthcare S.L.U. (Azacitidine Accord), betapharm Arzneimittel GmbH (Azacitidine betapharm), Bristol-Myers Squibb Pharma EEIG (Onureg, Vidaza), Mylan Ireland Limited (Azacitidine Mylan)

PRAC Rapporteur: Menno van der Elst

Scope: Signal of Cutaneous Vasculitis

Action: For adoption of PRAC recommendation

EPITT 19929 – New signal

Lead Member State(s): NL

4.1.2. Baricitinib – OLUMIANT (CAP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Signal of interstitial lung disease

Action: For adoption of PRAC recommendation

EPITT 19913 – New signal

Lead Member State(s): PL

4.1.3. Efgartigimod Alfa – VYVGART (CAP)

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Signal of anaphylactic reaction

Action: For adoption of PRAC recommendation

EPITT 19926 – New signal

Lead Member State(s): IE

[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

4.1.4. Latanoprost[3] (NAP)

Applicant: various

PRAC Rapporteur: to be appointed

Scope: Signal of choroidal detachment and Choroidal effusion

Action: For adoption of PRAC recommendation

EPITT 19936 – New signal

Lead Member State(s): BE

4.1.5. Mepolizumab – NUCALA (CAP)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of Arthralgia

Action: For adoption of PRAC recommendation

EPITT 19919 – New signal

Lead Member State(s): DE

4.1.6. Pirfenidone – ESBRIET (CAP), PIRFENIDONE AXUNIO (CAP), PIRFENIDONE VIATRIS (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Rhea Fitzgerald

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

Action: For adoption of PRAC recommendation

EPITT 19920 – New signal

Lead Member State(s): IE

4.2. New signals detected from other sources

4.2.1. Rituximab – BLITZIMA (CAP), MABTHERA (CAP), RIXATHON (CAP), RIXIMYO (CAP), RUXIENCE (CAP), TRUXIMA (CAP)

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

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of oral lichenoid reaction

Action: For adoption of PRAC recommendation

EPITT 19916 – New signal

[3] Except for products with paediatric indication

Lead Member State(s): DK

4.3. Signals follow-up and prioritisation

4.3.1. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/090

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of myositis

Action: For adoption of PRAC recommendation

EPITT 19884 – follow up to January 2023

4.3.2. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/004224/SDA/018; KISPLYX (CAP) - EMEA/H/C/003727/SDA/021

Applicant: Eisai GmbH

PRAC Rapporteur: Ulla Wändel Liminga (LENVIMA); David Olsen (KISPLYX)

Scope: Signal of adrenal insufficiency

Action: For adoption of PRAC recommendation

EPITT 19870 – follow up to January 2023

4.3.3. Progesterone (NAP)

Applicant: various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of meningioma

Action: For adoption of PRAC recommendation

EPITT 19871 – follow up to January 2023

4.3.4. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/SDA/063

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of myositis

Action: For adoption of PRAC recommendation

EPITT 19883 – follow up to January 2023

4.4. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Aflibercept - EMEA/H/C/006022

Scope: Treatment of age-related macular degeneration (AMD) and visual impairment

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

5.1.2. Cabotegravir - EMEA/H/C/005756

Scope: Pre-exposure prophylaxis of HIV-1 infection

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

5.1.3. Crisantaspase - EMEA/H/C/005917

Scope: Indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukaemia (ALL) and lymphoblastic lymphoma (LBL)

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

5.1.4. Dabrafenib - EMEA/H/C/005885, Orphan

Applicant: Novartis Europharm Limited

Scope: Treatment of glioma

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

5.1.5. Decitabine, cedazuridine - EMEA/H/C/005823, Orphan

Applicant: Otsuka Pharmaceutical Netherlands B.V.

Scope: Treatment of myeloid leukaemia

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

5.1.6. Elacestrant - EMEA/H/C/005898

Scope: Treatment of postmenopausal woman and men with breast cancer

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

5.1.7. Epcoritamab - EMEA/H/C/005985, Orphan

Applicant: AbbVie Deutschland GmbH & Co. KG

Scope: Treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL)

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

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

Applicant: Vertex Pharmaceuticals (Ireland) Limited, ATMP[4]

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

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

5.1.9. Masitinib - EMEA/H/C/005897, Orphan

Applicant: AB Science

Scope: In combination with riluzole for the treatment of adult patients with amyotrophic lateral sclerosis (ALS)

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

5.1.10. Oteseconazole - EMEA/H/C/005682

Scope: Treatment and prevention of recurrent vulvovaginal candidiasis (RVVC) including the acute episodes of RVVC in adult women

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

5.1.11. Palovarotene - SOHONOS (CAP MAA) - EMEA/H/C/004867, Orphan

Applicant: Ipsen Pharma

Scope (under re-examination): Treatment of fibrodysplasia ossificans progressive

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

5.1.12. Quizartinib - EMEA/H/C/005910, Orphan

Applicant: Daiichi Sankyo Europe GmbH

Scope : Treatment of adult patients with diagnosed acute myeloid leukaemia (AML)

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

5.1.13. Ritlecitinib - EMEA/H/C/006025

Scope: Treatment of severe alopecia areata in adults and adolescents 12 years of age and older

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

[4] Advanced therapy medicinal product

5.1.14. Sparsentan - EMEA/H/C/005783, Orphan

Applicant: Vifor France

Scope: Treatment of primary immunoglobulin A nephropathy (IgAN)

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

5.1.15. Sugammadex - EMEA/H/C/006115

Scope: Reversal of neuromuscular blockade induced by rocuronium or vecuronium

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

5.1.16. Tocilizumab - EMEA/H/C/005984

Scope: Treatment of rheumatoid arthritis, active systemic juvenile idiopathic arthritis (sJIA), juvenile idiopathic polyarthritis (pJIA), chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS) and COVID-19

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

5.1.17. Tocilizumab - EMEA/H/C/005781

Scope: Treatment of rheumatoid arthritis, active systemic juvenile idiopathic arthritis (sJIA), juvenile idiopathic polyarthritis (pJIA), giant cell arteritis (GCA), chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS) and COVID-19

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

5.1.18. Trametinib - EMEA/H/C/005886, Orphan

Applicant: Novartis Europharm Limited

Scope: Treatment of paediatric patients aged 1 year and older with glioma

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. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/II/0032

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 3.2 in order to reflect the updated study milestones and completion of the PASS of CE/BZA in the United States (US PASS, Study B2311060) previously assessed as part of II/0030 (MEA 002.15), as well as to update the post marketing data with the data lock point of 31 October 2021

Action: For adoption of PRAC Assessment Report

5.2.2. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/II/0039

Applicant: TEVA GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of an updated RMP version 4.0 in order to replace PASS TV48125-MH-50039 with PASS TV48125-MH-40217 following MEA/005.3 and MEA/005.4

Action: For adoption of PRAC Assessment Report

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

Applicant: Proveca Pharma Limited

PRAC Rapporteur: Zane Neikena

Scope: Submission of an updated RMP version 3.1 in order to remove study PRO/GLY/004: a drug utilisation study (DUS) to assess the efficacy of risk minimisation measures for Sialanar

Action: For adoption of PRAC Assessment Report

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Monica Martinez Redondo

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

Action: For adoption of PRAC Assessment Report

5.2.5. Measles, mumps, rubella and varicella vaccine (live) - PROQUAD (CAP) - EMEA/H/C/000622/WS2453/0160; Varicella vaccine (live) - ZOSTAVAX (CAP) - EMEA/H/C/000674/WS2453/0145

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of updated RMPs for ProQuad and Zostavax versions 8.1 and 10.1 respectively, in order to remove the Varicella Zoster Virus Identification Program (VZVIP) as a routine pharmacovigilance activity beyond adverse reactions reporting and signal detection from the RMP Part III: pharmacovigilance plan

Action: For adoption of PRAC Assessment Report

5.2.6. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS2434/0049; NEPARVIS (CAP) - EMEA/H/C/004343/WS2434/0047

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP version 5.0 for Ernestro and its duplicate marketing authorisation Neparvis to update the milestones for MEA 002 (study CLCZ696B2014) and MEA 004 (study CLCZ696B2015) from 31 December 2022 to 30 June 2024

Action: For adoption of PRAC Assessment Report

5.2.7. Tadalafil - TADALAFIL MYLAN (CAP) - EMEA/H/C/003787/WS2431/0023

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of an updated RMP (version 3) to develop follow-up forms in line with the reference product and to update Part III of RMP and Annex, Specific Adverse Drug Reaction Follow-up Forms accordingly, following CHMP and PRAC Rapporteurs Joint Assessment Report (EMEA/H/C/003787/R/0014, dated 15 April 2019); to adopt the safety concerns in the RMP in line with the ones available on CMDh website (Revision 35, dated Sep-2022) for generic RMP version 1.1 dated 01 April 2020 approved via procedure PT/H/1982/001-002/DC; to submit the updates in the new template (EMA/164014/2018 Rev.2.0.1 accompanying GVP Module V Rev.2)

Action: For adoption of PRAC Assessment Report

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

Applicant: SIGA Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

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

Action: For adoption of PRAC Assessment Report

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

5.3.1. Adalimumab - YUFLYMA (CAP) - EMEA/H/C/005188/X/0022

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to add a new strength (20 mg solution for injection). The indications for the new strength are identical to those already approved for the 40 mg strength. The RMP (version 2.1) has also been submitted. In addition, the MAH took the opportunity to include editorial changes in Mod. 2.3.A.1.2.2 and 3.2.A.1.2.2

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

5.3.2. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/II/0044, Orphan

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Extension of indication for the prevention of phototoxicity in adolescent patients (12 to under 18 years of age) with erythropoietic protoporphyria (EPP), based on the analysis of the safety and efficacy data available. As a consequence, sections 4.1, 4.2 and 4.4 of the SmPC are updated. The package leaflet is updated in accordance. Version 9.4 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce a minor editorial correction to the product information

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

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

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information following results from study PTC124-GD-041-DMD, listed as a specific obligation in the Annex II; this is a Phase 3 multicentre, randomised, double-blind, 18-month, placebo-controlled study, followed by a 18-month open label extension to confirm the efficacy and safety of ataluren in the treatment of ambulant patients with nonsense mutation Duchenne muscular dystrophy (mnDMD) aged 5 years or older. Annex II, and Annex IIB are updated to delete the SOB and to reflect the switch from conditional to full marketing authorisation. The package leaflet is updated accordingly. The RMP version 11.0 has also been submitted. Minor corrections were done to align the product information with the latest QRD templates

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

5.3.4. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/X/0035/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new strength (1 mg film-coated tablet), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment, as monotherapy or in combination with conventional synthetic disease modifying antirheumatic drugs (DMARDs), of active juvenile idiopathic arthritis (JIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more prior conventional synthetic or biologic DMARDs, based on final results from the pivotal study JAHV (I4V-MC-JAHV); this is a multicentre, double-blind, randomised, placebo-controlled,

medication-withdrawal Phase 3 study in children from 2 years to less than 18 years of age with JIA who have had an inadequate response or intolerance to treatment with at least 1 conventional DMARD (cDMARD) or biological (bDMARD). 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. Version 15.1 of the RMP has also been submitted

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

5.3.5. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0018

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to introduce an alternative posology regimen for wet age-related macular degeneration and update information based on modelling and simulation studies; the package leaflet is updated accordingly. The RMP version 9.0 has also been submitted

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

5.3.6. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0021

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendation in including an additional dose regimen (q16w) for diabetic macular edema (DME) patients during the maintenance phase, update the frequency of adverse drug reactions, update pharmacokinetic, pharmacodynamic, efficacy and safety information, following the assessment of procedure II/10, based on final results from studies CRTH258B2301 (KESTREL) and CRTH258B2302 (KITE). The package leaflet is updated accordingly. The RMP version 10 has also been submitted

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

5.3.7. Cerliponase alfa - BRINEURA (CAP) - EMEA/H/C/004065/II/0039, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Mari Thorn

Scope: Update of sections 4.2, 4.4, 4.8, 5.1, 5.2, 6.5 and 9 of the SmPC in order to state that clinical data are available for patients aged 1 year and older and to include updates to the frequency of adverse reactions, immunogenicity, pharmacokinetic, and paediatric population sections based on the final results from studies 190-203, listed as a specific obligation and 190-202 (submitted in P46/013). Study 190-203 was a Phase 2, open-label, multicentre study in pediatric patients < 18 years of age with CLN2 disease, confirmed by deficiency of TPP1 enzyme activity and mutation of the CLN2 gene. The package leaflet, Annex II and Annex IV are updated accordingly. The RMP version 4.0 has also been submitted

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

5.3.8. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0089

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of 'dizziness' and 'abdominal pain' in the list of adverse drug reactions (ADRs) to common and to update safety and efficacy information, based on final results and final pooled analysis for studies COV001, COV002, COV003 and COV005 as well as the final manuscript for COV004, listed as category 3 studies in the RMP. Study COV001 is phase I/II, single-blind, randomised, active-controlled, multicenter study in healthy adults aged 18-55 years; Study COV002 is a phase II/III, single-blind, randomised, active-controlled, multicenter study in adults ≥ 18 years of age and at high risk of exposure to COVID-19; Study COV003 is a phase III, single-blind, randomised, controlled, multicenter study in adults ≥ 18 years of age at high risk of exposure to SARS-CoV-2; Study COV005 is a phase I/II, double-blind, randomised, placebo-controlled, multicenter study in adults 18 to 65 years of age with or without HIV. Study COV004 a phase IB/II single-blind, randomised controlled trial of the (AZD1222) vaccine in adults in Kenya. The package leaflet is updated accordingly. The RMP version 7.0 has also been submitted

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

5.3.9. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0098

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Update of sections 4.2, 4.4, 5.1 and 5.2 in order to update efficacy, pharmacokinetic and safety information for paediatric population following the assessment of P46/043 and P46/044 based on final results from study 20130173, listed as a category 3 study in the RMP and study 20170534. Study 20130173 was a prospective, multicentre, open-label, single-arm phase 3 study to evaluate the safety, efficacy, and PK of denosumab in children 2 to 17 years of age with osteogenesis imperfecta (OI). Study 20170534 was an open-label, prospective, extension study of Study 20130173. The RMP version 31 has also been submitted. In addition, the MAH took this opportunity to introduce minor editorial changes

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

5.3.10. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP) - EMEA/H/C/002673/WS2438/0061/G; REVINTY ELLIPTA (CAP) - EMEA/H/C/002745/WS2438/0058/G

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Grouped application consisting of 1) Update sections 4.2 and 5.1 of the SmPC to include results from study HZA107116. This is a randomised, double-blind, parallel group, multicentre, stratified, study evaluating the efficacy and safety of once daily fluticasone furoate (FF)/vilanterol (VI) inhalation powder compared to once daily fluticasone furoate inhalation powder in the treatment of asthma in participants aged 5 to 17 years old

(inclusive) currently uncontrolled on inhaled corticosteroids. The package leaflet and labelling are updated accordingly. The RMP version 12.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC; 2) Submission of final report from Phase 2b study HZA106855 (FF dose ranging) which gives information regarding the dose selection for FF combination in study HZA107116; 3) Submission of final report from Phase 2b study HZA106853 (VI dose ranging) which gives information regarding the dose selection for VI combination in study HZA107116

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

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

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

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

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

5.3.12. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0113

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study CNTO148UCO1001 (PURSUIT PEDS PK) listed as a category 3 study in the RMP. This is a phase 1b open-label study to assess the safety and pharmacokinetics of subcutaneously administered golimumab, a human anti-TNFα antibody, in paediatric subjects with moderately to severely active ulcerative colitis. The RMP version 24.1 has also been submitted

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

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

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Gabriele Maurer

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

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

5.3.14. Ibandronic acid - BONDRONAT (CAP) - EMEA/H/C/000101/WS2451/0090; BONVIVA (CAP) - EMEA/H/C/000501/WS2451/0075

Applicant: Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add information regarding the risk of 'atypical fractures of long bones other than femour' based on literature. The package leaflet is updated accordingly. The RMP version 3.1 has also been submitted. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template version 10.3

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

5.3.15. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/X/0115/G

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Grouped variation consisting of: 1) Extension application to introduce a new strength (13.4 mg of ivacaftor granules in sachet), grouped with a type II variation (C.I.6.a) in order to extend the indication of the granule presentations to include children with cystic fibrosis (CF) aged 1 to less than 4 months of age and weighing 3 kg or more who have an R117H CFTR mutation or one of the approved 9 gating (class III) mutations based on interim results from study VX15-770-124 (study 124); this is a phase 3, 2-part, open-label study to evaluate the safety, pharmacokinetics, and pharmacodynamics of ivacaftor (IVA) in subjects with CF who are less than 24 months of age at treatment initiation and have a CFTR gating mutation. As a consequence, sections 1, 2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 6.3 and 8 of the SmPC of the granules presentations and sections 4.2, 4.8, 5.1 and 5.2 of the SmPC of the tablets presentations are updated. The labelling for the 13.4 mg granule presentation and the package leaflet of the granules and tablets presentations are updated in accordance. Version 15.2 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information; 2) other quality related variations

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

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

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

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

implement editorial changes in the SmPC

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

5.3.17. Maribavir - LIVTENCITY (CAP) - EMEA/H/C/005787/II/0004, Orphan

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from study SHP620-302 listed as a category 3 study in the RMP. This is a Phase III, multicentre, randomised, double-blind, double-dummy, active-controlled study of maribavir compared to valganciclovir for the treatment of asymptomatic cytomegalovirus (CMV) infection in hematopoietic stem cell transplant (HSCT) recipients. The RMP version 2.0 has also been submitted

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

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

Applicant: Nordic Group B.V.

PRAC Rapporteur: Martin Huber

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

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

5.3.19. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0130

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include OPDIVO for the adjuvant treatment of adults and adolescents 12 years of age and older with stage IIB or IIC melanoma who have undergone complete resection, based on results from study CA20976K; This is a phase III, randomised, double-blind study of adjuvant immunotherapy with nivolumab versus placebo after complete resection of stage IIB/C melanoma. 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 33.0 of the RMP has also been submitted

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

5.3.20. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/II/0013, Orphan

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of sections 4.4, 4.5 and 4.6 of the SmPC in order to update an existing warning, add drug-drug interaction (DDI) information with oral contraceptives and update

information for women of childbearing potential, based on study A4250-022 listed as a category 3 study in the RMP; this is an open-label, phase 1 DDI study to evaluate the interaction of odevixibat with oral lipophilic contraceptives in healthy volunteers. The package leaflet is updated accordingly. The RMP version 4.1 has also been submitted

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

5.3.21. Pandemic influenza vaccine (surface antigen, inactivated, adjuvanted) - FOCLIVIA (CAP) - EMEA/H/C/001208/II/0081

Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include children from 6 months to less than 18 years of age for Foclivia, based on final results from study V87_30; this is a phase 2, randomised, observer-blind, multicentre study to evaluate the immunogenicity and safety of several doses of antigen and MF59 adjuvant content in a monovalent H5N1 pandemic influenza vaccine in healthy pediatric subjects 6 months to less than 9 years of age. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated accordingly. Version 4.9 of the RMP 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

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

5.3.22. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0133

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include in combination with trastuzumab, fluoropyrimidine and platinum-containing chemotherapy for treatment of locally advanced unresectable or metastatic HER2- positive gastric or gastro-oesophageal junction adenocarcinoma for Keytruda, based on interim results from study KEYNOTE-811, an ongoing Phase 3, double-blind trial comparing trastuzumab plus chemotherapy and pembrolizumab with trastuzumab plus chemotherapy and placebo as first-line treatment in participants with HER2-positive advanced gastric or gastro-oesophageal junction adenocarcinoma. As a consequence, sections 4.1, 4.8, and 5.1 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. Version 40.1 of the RMP has also been submitted

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

5.3.23. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/II/0010

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy and safety information in the treatment of adult patients with RET fusion-positive advanced non-small cell lung cancer (NSCLC) based on final results (NSCLC indication) from study ARROW/BO42863, a phase 1/2 study of the highly-selective RET inhibitor, BLU 667, in

patients with thyroid cancer, NSCLC, and other advanced solid tumours listed as a specific obligation in the Annex II. The RMP version 1.5 has also been submitted

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

5.3.24. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0044/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendations for patients with renal impairment, remove an existing warning on renal impairment and update the safety and efficacy information based on final results from studies GS US 540 5912 and GS-US-540-9015, listed as category 3 studies in the RMP. Study GS US 540 5912 is a phase 3 randomised, double-blind, placebo-controlled, parallel group, multicentre study evaluating the efficacy and safety of remdesivir in participants with severely reduced kidney function who were hospitalised for COVID-19, while study GS-US-540-9015 is a phase 1, multicentre, open-label, single-dose study to evaluate the single-dose pharmacokinetic (PK) of remdesivir in participants with normal and impaired renal function. The package leaflet is updated accordingly. The RMP version 5.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor edits to the product information

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

5.3.25. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/II/0037

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information and the list of adverse drug reactions (ADRs) based on the final results from study CO-338-014 (ARIEL 3) listed as a category 1 PAES in the Annex II; this is a phase 3, multicentre, randomised, double-blind, placebo-controlled study of rucaparib as switch maintenance following platinum-based chemotherapy in patients with platinum-sensitive, high grade serous or endometrioid epithelial ovarian, primary peritoneal or fallopian tube cancer. The package leaflet is updated accordingly. The RMP version 6.4 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

5.3.26. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS2465/0051; NEPARVIS (CAP) - EMEA/H/C/004343/WS2465/0049

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final report from study CLCZ696B2320 listed as a category 3 study in the RMP in order to fulfil MEA/001. This is a multicentre, randomised, double-blind, active-controlled study to evaluate the effects of LCZ696 compared to valsartan on cognitive

function in patients with chronic heart failure and preserved ejection fraction. The RMP version 6 has also been submitted

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

5.3.27. Sodium phenylbutyrate - PHEBURANE (CAP) - EMEA/H/C/002500/X/0035

Applicant: Eurocept International B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (350 mg/ml oral solution). The RMP (version 0.1) is updated in accordance

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

5.3.28. Sotorasib - LUMYKRAS (CAP) - EMEA/H/C/005522/II/0010/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.2, 4.4, 4.8, 5.2 and 5.3 of the SmPC in order to change in the recommended dose and to update safety and efficacy information based on results from study 20190009 (CodeBreaK 200) listed as a specific obligation in the Annex II, in order to fulfil SOB/001; and results from study 20170543 (CodeBreak 100) phase 2 part B. Study 20190009 is a phase 3 multicentre, randomised, open-label, active-controlled study of AMG 510 versus docetaxel for the treatment of previously treated locally advanced and unresectable or metastatic non-small cell lung cancer (NSCLC) subjects with mutated KRAS p.G12C; while study 20170543 is a phase 1/2, open-label study evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of AMG 510 monotherapy in subjects with advanced solid tumours with KRAS p.G12C mutation and AMG 510 combination therapy in subjects with advanced NSCLC with KRAS p.G12C mutation. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to update Annex II of the SmPC

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

5.3.29. Tafasitamab - MINJUVI (CAP) - EMEA/H/C/005436/II/0008, Orphan

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 of the SmPC in order to add a new warning on progressive multifocal leukoencephalopathy (PML) based on post-marketing data; the package leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and to bring the product information in line with the latest QRD template version 10.3

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

5.3.30. Trientine - CUFENCE (CAP) - EMEA/H/C/004111/X/0014/G

Applicant: Univar Solutions BV

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension application to add a new strength (100 mg capsule, hard) grouped with a type IA variation (B.II.b.4.b) to introduce an alternate blend batch size range. The RMP (version 1.3) is updated in accordance. The marketing authorisation holder took the opportunity to align the product information to the latest QRD template (version 10.3)

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

5.3.31. Trifluridine, tipiracil - LONSURF (CAP) - EMEA/H/C/003897/II/0026

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of patients with refractory metastatic colorectal cancer, for LONSURF in combination with bevacizumab based on results from study SUNLIGHT (CL3-95005-007). This is an open-label, randomised, phase III study comparing trifluridine/tipiracil in combination with bevacizumab to trifluridine/tipiracil monotherapy in patients with refractory metastatic colorectal cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC. The package leaflet is updated in accordance. The updated RMP version 9.1 has also been submitted. In addition, the MAH took the opportunity to update section 4.6 of the SmPC and the package leaflet accordingly

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

5.3.32. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0098/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: –Grouped variations consisting of : 1) to add a new pre-filled pen (PFP) presentation, for Stelara 45 mg solution for injection (EU/1/08/494/00x); 2) to add a new PFP presentation for Stelara 90 mg Solution for injection (EU/1/08/494/00x); The RMP (Version 23.3) has been updated

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

5.3.33. Vosoritide - VOXZOGO (CAP) - EMEA/H/C/005475/II/0007, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: Type II B. IV.1.z Change of a measuring or administration device: to register an alternative CE-marked Transfer Needle and Administration Syringe from an alternate supplier, with consequential changes to the instructions for use in the product information (SmPC and PL)

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

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

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study BGB-3111-113 - a drug-drug interaction study of zanubrutinib with moderate and strong CYP3A inhibitors in patients with B-cell malignancies, listed as a category 3 study in the RMP. The RMP version 3.0 has also been submitted

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Andexanet alfa - ONDEXXYA (CAP) - PSUSA/00010764/202210

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Asciminib - SCEMBLIX (CAP) - PSUSA/00011008/202210

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Axicabtagene ciloleucel - YESCARTA (CAP) - PSUSA/00010703/202210

Applicant: Kite Pharma EU B.V., ATMP[5]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.4. Bezlotoxumab - ZINPLAVA (CAP) - PSUSA/00010576/202210

Applicant: Merck Sharp & Dohme B.V.

[5] Advanced therapy medicinal product

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Brolucizumab - BEOVU (CAP) - PSUSA/00010829/202210

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Bupivacaine[6] - EXPAREL LIPOSOMAL (CAP) - PSUSA/00010889/202210

Applicant: Pacira Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Cariprazine - REAGILA (CAP) - PSUSA/00010623/202210

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Chenodeoxycholic acid[7] [8] - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - PSUSA/00010590/202210

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Choriogonadotropin alfa - OVITRELLE (CAP) - PSUSA/00000736/202209

Applicant: Merck Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

[6] Liposomal formulations only
[7] Indicated for the treatment of inborn errors of primary bile acid synthesis due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis (CTX)) in infants, children and adolescents aged 1 month to 18 years and adults
[8] Centrally authorised product(s) only

Action: For adoption of recommendation to CHMP

6.1.10. Conestat alfa - RUCONEST (CAP) - PSUSA/00000873/202210

Applicant: Pharming Group N.V

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Dapagliflozin - EDISTRIDE (CAP); FORXIGA (CAP) - PSUSA/00010029/202210

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Delamanid - DELTYBA (CAP) - PSUSA/00010213/202210

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Dostarlimab - JEMPERLI (CAP) - PSUSA/00010931/202210

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Edoxaban - LIXIANA (CAP); ROTEAS (CAP) - PSUSA/00010387/202210

Applicant: Daiichi Sankyo Europe GmbH (Lixiana), Berlin Chemie AG (Roteas)

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Glycopyrronium bromide[9] - ENUREV BREEZHALER (CAP); SEEBRI BREEZHALER (CAP); TOVANOR BREEZHALER (CAP) - PSUSA/00010047/202209

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - PSUSA/00010678/202210

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Histamine[10] - CEPLENE (CAP) - PSUSA/00001610/202210

Applicant: Laboratoires Delbert

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Insulin degludec, liraglutide - XULTOPHY (CAP) - PSUSA/00010272/202209

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Irinotecan[11] - ONIVYDE PEGYLATED LIPOSOMAL (CAP) - PSUSA/00010534/202210

Applicant: Les Laboratoires Servier

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] Centrally authorised product(s) indicated for chronic obstructive pulmonary disease
[10] Indicated for acute myeloid leukemia
[11] Liposomal formulation(s) only

6.1.20. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - PSUSA/00010868/202210

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Lasmiditan - RAYVOW (CAP) - PSUSA/00011011/202210

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Micafungin - MYCAMINE (CAP) - PSUSA/00002051/202210

Applicants: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Nintedanib[12] - OFEV (CAP) - PSUSA/00010319/202210

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - FOCLIVIA (CAP); prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - PSUSA/00010008/202210

Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Parathyroid hormone - NATPAR (CAP) - PSUSA/00010591/202210

Applicant: Takeda Pharmaceuticals International AG

[12] Respiratory indication(s) only

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Pemigatinib - PEMAZYRE (CAP) - PSUSA/00010923/202210

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Ranibizumab - BYOOVIZ (CAP); LUCENTIS (CAP); RANIVISIO (CAP) - PSUSA/00002609/202210

Applicant: Samsung Bioepis NL B.V. (Byooviz), Novartis Europharm Limited (Lucentis), Midas Pharma GmbH (Ranivisio)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Rivaroxaban - XARELTO (CAP) - PSUSA/00002653/202209

Applicant: Bayer AG

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Sacituzumab govitecan - TRODELVY (CAP) - PSUSA/00010959/202210

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Selumetinib - KOSELUGO (CAP) - PSUSA/00010936/202210

Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Somatrogon - NGENLA (CAP) - PSUSA/00010982/202210

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Talazoparib - TALZENNA (CAP) - PSUSA/00010781/202210

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/202210

Applicant: Amgen Europe B.V., ATMP[13]

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.34. Tobramycin[14] [15] - VANTOBRA (CAP) - PSUSA/00010370/202209

Applicant: PARI Pharma GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Tucatinib - TUKYSA (CAP) - PSUSA/00010918/202210

Applicant: Seagen B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Vandetanib - CAPRELSA (CAP) - PSUSA/00009327/202210

Applicant: Genzyme Europe BV

PRAC Rapporteur: Tiphaine Vaillant

[13] Advanced therapy medicinal product
[14] Nebuliser solution
[15] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Vortioxetine - BRINTELLIX (CAP) - PSUSA/00010052/202209

Applicant: H. Lundbeck A/S

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. Anagrelide - ANAGRELIDE MYLAN (CAP); XAGRID (CAP); NAP - PSUSA/00000208/202209

Applicants: Mylan Pharmaceuticals Limited (Anagrelide Mylan), Takeda Pharmaceuticals International AG Ireland Branch (Xagrid), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Posaconazole - NOXAFIL (CAP); NAP - PSUSA/00002480/202210

Applicants: Merck Sharp & Dohme B.V. (Noxafil), various

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Sodium oxybate[16] - XYREM (CAP); NAP - PSUSA/00010612/202210

Applicants: UCB Pharma S.A. (Xyrem), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Thalidomide - THALIDOMIDE BMS (CAP); THALIDOMIDE LIPOMED (CAP); NAP - PSUSA/00002919/202210

Applicants: Bristol-Myers Squibb Pharma EEIG (Thalidomide BMS), Lipomed GmbH

[16] Oral use only

(Thalidomide Lipomed), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. ^{13}C-methacetin (NAP) - PSUSA/00010846/202210

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Ambroxol (NAP) - PSUSA/00000130/202209

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Ambroxol, clenbuterol (NAP) - PSUSA/00000131/202209

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Aminosalicylic acid (NAP) - PSUSA/00000165/202210

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Artemether, lumefantrin[17] (NAP) - PSUSA/00000236/202210

Applicant(s): various

[17] All except dispersible tablet(s)

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Bromhexine (NAP) - PSUSA/00000437/202209

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Carbidopa, levodopa (NAP) - PSUSA/00000548/202210

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Clenbuterol (NAP) - PSUSA/00000794/202209

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Dinoprostone (NAP) - PSUSA/00001104/202209

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Etidronate (NAP) - PSUSA/00001320/202209

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Etomidate (NAP) - PSUSA/00001330/202209

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Famotidine (NAP) - PSUSA/00001350/202209

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Felbamate (NAP) - PSUSA/00010155/202209

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Fenoterol[18] (NAP) - PSUSA/00001366/202209

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Lysine acetylsalicylate (NAP) - PSUSA/00001921/202209

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Polystyrene sulfonate (NAP) - PSUSA/00002472/202210

Applicant(s): various

PRAC Lead: Jana Lukačišinová

[18] Respiratory indication(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Ropivacaine (NAP) - PSUSA/00002662/202209

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Terbinafine (NAP) - PSUSA/00002896/202209

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Trifarotene (NAP) - PSUSA/00010929/202210

Applicant(s): various

PRAC Lead: Mari Thörn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/LEG 007.1

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 007 [Causality assessment of pneumonia cases already reported as confounded by the MAH as well as of any newly reported cases, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010180/202111) adopted in July 2022] as per request for supplementary information (RSI) adopted in December 2022

Action: For adoption of advice to CHMP

6.4.2. Cabozantinib - COMETRIQ (CAP) - EMEA/H/C/002640/LEG 022.1

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 022 [Causality assessment of pneumonia cases already reported as confounded by the MAH as well as of any newly reported cases, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010180/202111) adopted in July 2022] as per request for supplementary information (RSI) adopted in December 2022

Action: For adoption of advice to CHMP

6.4.3. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/LEG 008

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the seventh periodic benefit-risk evaluation report covering the reporting interval of 06 July 2021 to 05 July 2022 together with the WHO-UMC causality of additional cases and drug-induced liver injury signal investigation as requested in the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00010697/202207) adopted in February 2023

Action: For adoption of advice to CHMP

6.4.4. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/LEG 009

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a DHPC (Direct Health Care Professional Communication) and a communication plan aiming at informing health care professionals about the risk of tuberculosis and the measures as requested in the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00010961/202209) adopted in April 2023

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - EMEA/H/C/005737/II/0072/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 of the SmPC in order to add a new warning on pericarditis and myocarditis and update of section 4.8 of the SmPC to add myocarditis and pericarditis to the list of adverse drug reactions (ADRs) with frequency not known based on post-marketing data and three observational claims databases in US as requested in the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00010916/202208) adopted in April 2023. The package leaflet is updated accordingly. The RMP version 6.2 has also been submitted. In addition, the MAH took the opportunity to update the ATC Code as amended by the WHO

Action: For adoption of PRAC Assessment Report

6.5.2. Nirmatrelvir, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/II/0032

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC in order to add 'hypertension' to the list of adverse drug reactions (ADRs) with frequency 'uncommon', following procedure EMEA/H/C/005973/LEG 006 (LEG assessed by PRAC), based on review of aggregated post-marketing data. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[19]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[20]

7.1.1. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - EMEA/H/C/PSA/S/0103

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Substantial amendment to a Cerebrotendinous Xanthomatosis Registry: long term non-interventional follow-up of safety and effectiveness of Chenodeoxycholic Acid Leadiant

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

7.1.2. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/PSA/S/0104

Applicant: Janssen-Cilag International NV, ATMP[21]

PRAC Rapporteur: Jo Robays

Scope: Substantial amendment to a PASS study 68284528MMY4009 protocol to evaluate the safety of multiple myeloma patients treated with ciltacabtagene autoleucel

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

7.1.3. Lonafarnib - ZOKINVY (CAP) - EMEA/H/C/PSP/S/0102.1

Applicant: EigerBio Europe Limited

[19] 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
[20] In accordance with Article 107n of Directive 2001/83/EC
[21] Advanced therapy medicinal product

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to PSP/0102 [Prospective observational study to evaluate the long-term safety and effectiveness of lonafarnib treatment among patients with Hutchinson-Gilford Progeria Syndrome (HGPS) or a processing deficient progeroid laminopathy (PDPL) in real-world clinical care settings] as per the request to supplementary information (RSI) adopted in December 2022

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

7.1.4. Tabelecleucel - EBVALLO (CAP) - EMEA/H/C/PSP/S/0104

Applicant: Pierre Fabre Medicament, ATMP[22]

PRAC Rapporteur: Amelia Cupelli

Scope: An observational PASS to describe the safety and effectiveness of tabelecleucel in patients with Epstein-Barr Virus positive (EBV+) Post-Transplant Lymphoproliferative Disease (PTLD) in a real-world setting in Europe

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

7.1.5. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/PSA/S/0100.1

Applicant: Novartis Europharm Limited, ATMP[23]

PRAC Rapporteur: Gabriele Maurer

Scope: Substantial amendment to a protocol for a registry study to assess the long-term safety of patients with B lymphocyte malignancies treated with tisagenlecleucel [MAH's response to PSA/S/0100]

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[24]

7.2.1. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 004.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 004.1 [Protocol for study B7451015: an adolescent imaging substudy to evaluate if abrocitinib has any clinically meaningful effects on bone growth and development] as per the request to supplementary information (RSI) adopted in January 2023

Action: For adoption of advice to CHMP

[22] Advanced therapy medicinal product
[23] Advanced therapy medicinal product
[24] 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. Anifrolumab - SAPHNELO (CAP) - EMEA/H/C/004975/MEA 002.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002 [Protocol for study D3461R00046: a non-interventional cohort study and meta-analysis on the risk of malignancy in systemic lupus erythematosus patients receiving anifrolumab] as per the request to supplementary information (RSI) adopted in December 2022

Action: For adoption of advice to CHMP

7.2.3. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 072.1

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: MAH's response to MEA 0072 [Protocol for study mRNA-1273-P919 (listed as category 3 study in the RMP): an observational study to assess maternal and infant outcomes following exposure to Spikevax during pregnancy and to assess whether the rate of pregnancy complications, adverse pregnancy outcomes, or adverse neonatal outcomes is associated with prenatal exposure to Spikevax] as per the request to supplementary information (RSI) adopted in January 2023

Action: For adoption of advice to CHMP

7.2.4. Eptinezumab - VYEPTI (CAP) - EMEA/H/C/005287/MEA 004.2

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 004.1 [protocol for study 19756N: a long-term cardiovascular safety and real-world use of eptinezumab - an observational, historical cohort study of patients initiating eptinezumab in routine clinical practice] as per request for supplementary information (RSI) adopted in December 2022

Action: For adoption of advice to CHMP

7.2.5. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/MEA 006.4

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Amendment to a previously agreed protocol for study ALN-AS1-006: a global observational longitudinal prospective registry of patients with acute hepatic porphyria (AHP) [ELEVATE]]

Action: For adoption of advice to CHMP

7.2.6. Inebilizumab - UPLIZNA (CAP) - EMEA/H/C/005818/MEA 001.1

Applicant: Horizon Therapeutics Ireland DAC

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 001 [protocol for an observational pregnancy safety study in women with neuromyelitis optica spectrum disorder (NMOSD) exposed to Uplizna (ineblizumab)] as per the request for supplementary information (RSI) adopted in November 2022

Action: For adoption of advice to CHMP

7.2.7. Inebilizumab - UPLIZNA (CAP) - EMEA/H/C/005818/MEA 003.1

Applicant: Horizon Therapeutics Ireland DAC

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 003 [protocol for a real-world observational study of outcomes for patients with neuromyelitis optica spectrum disorder (NMOSD) treated With inebilizumab in Europe] as per the request for supplementary information (RSI) adopted in November 2022

Action: For adoption of advice to CHMP

7.2.8. Inebilizumab - UPLIZNA (CAP) - EMEA/H/C/005818/MEA 004.1

Applicant: Horizon Therapeutics Ireland DAC

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 004 [protocol for a safety study of patients with neuromyelitis optica spectrum disorder (NMOSD) patients receiving inebilizumab following closure of the open-label period (N-MOmentum LT)] as per the request for supplementary information (RSI) adopted in November 2022

Action: For adoption of advice to CHMP

7.2.9. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 071.3

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: MAH's response to MEA 071.2 [feasibility assessment report for study OXON 214-04 (listed as a category 3 study in the RMP): an observational study utilising data from EU national multiple sclerosis (MS) registries to estimate the incidence of anti-natalizumab antibody among patients who receive subcutaneous administration (SC) of natalizumab for treatment of relapsing remitting MS in order to investigate immunogenic potential of SC administration (PASS 101MS412) (from X/0116)] as per the request for supplementary information (RSI) adopted in December 2022

Action: For adoption of advice to CHMP

7.2.10. Ponesimod - PONVORY (CAP) - EMEA/H/C/005163/MEA 004.3

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 004.2 [protocol for study PCSNSP003693 (listed as a category 3 study in the RMP): a survey among healthcare professionals (neurologists treating patients with multiple sclerosis (MS) along with MS specialist nurses) in selected European countries to evaluate knowledge and behaviours required for the safe use of ponesimod] as per the request for supplementary information (RSI) adopted in November 2022

Action: For adoption of advice to CHMP

7.2.11. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 010

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for a long-term comparative cohort study in patients with Crohn's disease in a real world setting to obtain additional long-term data from the real-world experience of patients with Crohn's disease treated with risankizumab to assess product potential risks and to estimate rates of malignancy (malignancy excluding non-melanoma skin cancer (NMSC), serious infections, serious hypersensitivity reactions, and major adverse cardiovascular events (MACE) in risankizumab treated patients with Crohn's disease, relative to alternative systemic therapies (e.g., biologics)

Action: For adoption of advice to CHMP

7.2.12. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.7

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Protocol amendment to a previously agreed protocol for clinical study C4591012 to assess the occurrence of safety events of interest, including severe or atypical COVID-19 in real-world use of COVID-19 mRNA vaccine

Action: For adoption of advice to CHMP

7.2.13. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 064

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for a non-interventional post-approval safety study of Pfizer-BioNTech bivalent COVID-19 vaccine in the United States in order to fulfill MAH commitment within PAM MEA-011.7 based on the outcome of procedure EMEA/H/C/005735/II/0143 regarding the Agency's request related to protocol amendments for on-going PASS with Omicron BA.1 and BA.4-5

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[25]

7.3.1. Valproate[26] (NAP) - EMEA/H/N/PSR/J/0043

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

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

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

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

7.4.1. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0111

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from year 5 Post-Treatment Follow-Up from study BEL 115467/HGS1006-C113 listed as a category 3 study in the RMP. This is a 52-week, global, multi-center, randomised, placebo-controlled, double-blind study conducted to evaluate mortality and AESI in adults with active, autoantibody-positive SLE treated with belimumab plus standard therapy vs. placebo plus standard therapy. Following the 52-week controlled treatment period (Year 1), the study included a 4-year follow-up of each participant (Year 2-5). During the follow-up period, participants no longer received study intervention. The RMP version 44 has also been submitted

Action: For adoption of PRAC Assessment Report

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

Applicant: Almirall S.A

PRAC Rapporteur: Mari Thorn

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

Action: For adoption of PRAC Assessment Report

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

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

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

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

Action: For adoption of PRAC Assessment Report

7.4.4. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0085/G

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Grouped application comprising two type II variations as follows: 1) To add Spikevax bivalent Original/ Omicron BA.4-5 vaccine (mRNA-1273.222), to update studies mRNA-1273-P904, mRNA-1273-P905 and mRNA-1273-P910 in the Pharmacovigilance Plan to include exposure to Spikevax bivalent vaccines, to update the INN to elasomeran/davesomeran, and to reclassify studies mRNA-1273-P205 from category 2 to category 3 studies in the Pharmacovigilance Plan; 2) To submit the final CSR from study mRNA-1273-P201, a Phase 2a, Randomised, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults ≥= 18 Years listed as a category 3 study including addition of clinical trial exposure data for part C of the study mRNA-1273-P201. RMP version 6.0 will be updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0111

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.6 of the SmPC in order to update information on pregnancy based on final results from PASS study CNTO148ART4001 listed as a category 3 study in the RMP; this is an observational prospective cohort study to collect and analyse information pertaining to pregnancy outcomes of women exposed to golimumab during pregnancy. The RMP version 23.2 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.6. Human papillomavirus 9-valent vaccine (recombinant, adsorbed) - GARDASIL 9 (CAP) - EMEA/H/C/003852/II/0063

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.6 of the SmPC in order to include additional information on exposure during pregnancy, based on the final report of the US Pregnancy Registry, listed as a category 3 study in the RMP; the package leaflet is updated accordingly. The RMP version 5.1 has also been submitted

Action: For adoption of PRAC Assessment Report

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

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

Action: For adoption of PRAC Assessment Report

7.4.8. Voriconazole - VFEND (CAP); NAP - EMEA/H/C/000387/WS2270/0147

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of Annex II and RMP to version 6.0 to include the results from final clinical study report (CSR) following the completion of a non-interventional (NI) PASS A1501103: an active safety surveillance program to monitor selected events in patients with long-term voriconazole use - MEA091. In addition, MAH is also taking this opportunity to introduce editorial changes [in fulfilment of MEA 091.5]

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. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 048.11

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual update report on recruitment for study IM101240 (listed as a category 3 study in the RMP): an observational registry of abatacept in patients with juvenile idiopathic arthritis (JIA registry) to explore the long-term safety of abatacept treatment for JIA in routine clinical practice by quantifying the incidence rates of serious infections, autoimmune

disorders and malignancies [final registry report expected by 2029]

Action: For adoption of advice to CHMP

7.5.2. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.18

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Ninth annual interim report for study BEL116543/HGS1006-C1124 (SABLE): a long-term controlled safety registry evaluating the incidence of all-cause mortality and adverse events of special interest (AESIs) in patients with systemic lupus erythematosus followed for a minimum of 5 years

Action: For adoption of advice to CHMP

7.5.3. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 003.10

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Eighth interim report for study P903 (listed as a category 3 study in the RMP): a PASS of Spikevax (elasomeran) in the US - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals

Action: For adoption of advice to CHMP

7.5.4. Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/MEA 001.2

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Interim report for study CAMG334A2023: a non-interventional study to examine patient characteristics and drug utilisation patterns in migraine patients treated with prophylactic drugs in the Nordic registries [final clinical study report (CSR) expected end of data collection + 1 year]

Action: For adoption of advice to CHMP

7.5.5. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 001.8

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual progress report 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

7.5.6. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/MEA 014.5

Applicant: Eisai GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second annual study progress report for study E7080-M000-508: an observational study to characterise hepatic related toxicity and overall safety profile in real-life conditions in the EU (Western population) in hepatocellular carcinoma (HCC) patients, including patients with Child-Pugh B

Action: For adoption of advice to CHMP

7.5.7. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 003.5

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 003.4 to second interim study report for ALN-TTR02-010: patisiran- lipid nanoparticle (LNP) pregnancy surveillance programme (PSP) to collect primary data on pregnant women from the US, the United Kingdom (UK), France, Spain, Italy, Portugal and Germany, and other potential countries, who have been exposed to patisiran during the exposure window, defined as 12 weeks prior to their last menstrual period (LMP), or at any time during pregnancy as well as to collect and analyse information pertaining to pregnancy complications and birth outcomes in women exposed to patisiran during pregnancy, as per the request for supplementary information (RSI) as adopted in January 2023

Action: For adoption of advice to CHMP

7.5.8. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 054.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study C4591022 [Pfizer-BioNTech COVID-19 Vaccine exposure during pregnancy: a non-interventional post-approval safety study of pregnancy and infant outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry]

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/ANX 009.2

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: The provision of answers to questions about the feasibility report of the non-interventional PASS to investigate the risk of mortality in multiple sclerosis (MS) patients

treated with alemtuzumab (Lemtrada) relative to comparable MS patients using other disease modifying treatments (DMTs) as requested in the new EMEA/H/C/003718/ANX/0009.1

Action: For adoption of advice to CHMP

7.6.2. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/REC 004.2

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: MAH's response to REC 004.1 [submission of an addendum to the final clinical report for study (17712): efficacy and safety study of darolutamide (ODM-201) in men with high-risk non-metastatic castration-resistant prostate cancer (ARAMIS)] as per request for supplementary information (RSI) adopted in December 2022

Action: For adoption of advice to CHMP

7.6.3. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/LEG 017.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: From II-0031: Commitment to provide targeted tumour lysis syndrome (TLS) assessment reports on a biannual basis (submitted annually within the PSUR, and 6 months after the PSUR submission in a separate report) through 2023, and annually thereafter, as per the RMP v8.0. These biannual assessment reports ensure close monitoring of the important identified risk of TLS, and the evaluation of the impact of newly implemented risk minimisation measures for TLS, on adherence to both already existing and updated recommendation added to the SmPC, the impact of the DHPC distributed to hematologists, and the patient card

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Glucarpidase - VORAXAZE (CAP) - EMEA/H/C/005467/S/0013 (without RMP)

Applicant: SERB S.A.S.

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Tecovirimat - TECOVIRIMAT SIGA (CAP) - EMEA/H/C/005248/S/0004 (without RMP)

Applicant: SIGA Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

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

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/R/0025 (without RMP)

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Budesonide - KINPEYGO (CAP) - EMEA/H/C/005653/R/0003 (without RMP)

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Larotrectinib - VITRAKVI (CAP) - EMEA/H/C/004919/R/0031 (without RMP)

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.5. Tafasitamab - MINJUVI (CAP) - EMEA/H/C/005436/R/0009 (without RMP)

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.6. Teclistamab - TECVAYLI (CAP) - EMEA/H/C/005865/R/0002 (without RMP)

Applicant: Janssen-Cilag International N.V.

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. Adalimumab - HULIO (CAP) - EMEA/H/C/004429/R/0041 (without RMP)

Applicant: Viatris Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/R/0056 (with RMP)

Applicant: Kite Pharma EU B.V., ATMP[28]

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

[28] Advanced therapy medicinal product

8.3.3. Brigatinib - ALUNBRIG (CAP) - EMEA/H/C/004248/R/0049 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Camurus AB

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/R/0023 (with RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Meropenem, vaborbactam - VABOREM (CAP) - EMEA/H/C/004669/R/0019 (without RMP)

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Paclitaxel - APEALEA (CAP) - EMEA/H/C/004154/R/0017 (with RMP)

Applicant: Inceptua AB

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Pegfilgrastim - FULPHILA (CAP) - EMEA/H/C/004915/R/0042 (without RMP)

Applicant: Viatris Limited

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Radium (Ra^{223}) - XOFIGO (CAP) - EMEA/H/C/002653/R/0049 (with RMP)

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/R/0042 (with RMP)

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Vestronidase alfa - MEPSEVII (CAP) - EMEA/H/C/004438/R/0033 (without RMP)

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: BioMarin International Limited, ATMP[29]

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.3.15. Voretigene neparvovec - LUXTURNA (CAP) - EMEA/H/C/004451/R/0040 (without RMP)

Applicant: Novartis Europharm Limited, ATMP[30]

PRAC Rapporteur: Gabriele Maurer

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

9.1.1. Risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders connected with human centrally authorised products

Scope: Pharmacovigilance inspection programme 2023-2026 (first revision for 2023)

Action: For adoption

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

[29] Advanced medicinal therapy product
[30] Advanced therapy medicinal product

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Ibandronic acid - BONDRONAT (CAP) - EMEA/H/C/000101/WS2451/0090; BONVIVA (CAP) - EMEA/H/C/000501/WS2451/0075

Applicant: Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: PRAC consultation on a worksharing variation procedure to update the product information of Bonviva and Bondronat regarding the risk of 'atypical fractures of long bones other than femour' based on literature

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q1 2023

Action: For information

12.1.3. PRAC assessors' trainings – organisational matters

PRAC lead: Martin Huber

Action: For discussion

12.1.4. Vote by proxy

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.4.2. PRAC strategic review and learning meeting (SRLM) under the Swedish presidency of the European Union (EU) Council – Uppsala, Sweden, 24 - 26 May 2023 - agenda

PRAC lead: Ulla Wändel Liminga, Mari Thorn

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q1 2023 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q1 2023

Action: For discussion

12.8.3. MAAs 3-year forecast report for March 2023 - December 2025

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.10.5. Periodic safety update reports single assessment (PSUSA) – review of 'other considerations' section in the assessment report - update and proposed way forward

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.14.3. Risk management plan (RMP) of medicinal product(s) - publication on EMA website

Action: For discussion

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

12.20.1. Study of exposure and use patterns of alternatives to ranitidine-containing medicines in patients treated with ranitidine - PRAC Sponsors critical appraisal

PRAC lead: David Olsen

Action: For discussion

12.20.2. Study on the impact of EU label changes for fluoroquinolone-containing medicinal products for systemic and inhalation use: post-referral prescribing trends – finalisation of DHPC and communication plan

PRAC lead: Eva Jirsová, Martin Huber

Action: For discussion

12.21. Others

12.21.1. Haematology WP reflection paper on novel therapies for Haemophilia

Action: For discussion

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

Action: For discussion

12.21.3. Report on experience with Real World Evidence (RWE) studies to support EMA scientific committees

Action: For discussion

13. Any other business

Next meeting on: 05-08 June 2023

14. Explanatory notes

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

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

(Items 2 and 3 of the PRAC agenda)

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

Signals assessment and prioritisation

(Item 4 of the PRAC agenda)

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC agenda)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC agenda)

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC agenda)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC agenda)

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

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