29 August 2022
EMA/PRAC/626661/2022
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 29 August - 01 September 2022

Chair: Sabine Straus – Vice-Chair: Martin Huber

29 August 2022, 10:30 – 19:30, via teleconference

30 August 2022, 08:30 – 19:30, via teleconference

31 August 2022, 08:30 – 19:30, via teleconference

01 September 2022, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

15 September 2022, 09:00 – 12:00, via teleconference

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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 29 August - 01 September 2022. See September 2022 PRAC minutes (to be published post October 2022 PRAC meeting).

1.2. Agenda of the meeting on 29 August - 01 September 2022

Action: For adoption

1.3. Minutes of the previous meeting on 04-07 July 2022

Action: For adoption

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

2.1. Newly triggered procedures

2.1.1. Pholcodine (NAP); pholcodine, biclotymol, chlorphenamine (NAP); pholcodine, chlorphenamine (NAP); pholcodine, chlorphenamine, ephedrine (NAP); pholcodine, diphenhydramine (NAP); pholcodine, dextromethorphan, paracetamol (NAP); pholcodine, diphenhydramine, paracetamol, pseudoephedrine (NAP); pholcodine, guaiacol (NAP); pholcodine, paracetamol, pseudoephedrine (NAP) - EMEA/H/A-107i/1521

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 107i of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption of a list of questions

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

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. Janus kinase (JAK) inhibitors[1]: abrocitinib - CIBINQO (CAP); baricitinib - OLUMIANT (CAP); filgotinib - JYSELECA (CAP); tofacitinib - XELJANZ (CAP); upadacitinib - RINVOQ (CAP) – EMEA/H/A-20/1517

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Rinvoq), Eli Lilly Nederland B.V. (Olumiant), Galapagos N.V. (Jyseleca), Pfizer Europe MA EEIG (Cibinqo, Xeljanz)

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur(s): Liana Gross-Martirosyan (Olumiant, Xeljanz), Nikica Mirošević Skvrce (Cibinqo, Jyseleca, Rinvoq)

Scope: Review of the benefit-risk balance following notification by the European Commission (EC) of a referral under Article 20 of Regulation (EC) No 726/2004, based on pharmacovigilance data

Action: For endorsement of a list of experts for the ad-hoc expert group (AHEG) meeting

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

3.4.1. Amfepramone (NAP) - EMEA/H/A-31/1501

Applicant(s): Artegodan GmbH, Temmler Pharma GmbH

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

Scope: Request for re-examination under Article 32 of Directive 2001/83/EC of the benefit-risk balance following notification by Romania of a referral under Article 31 of Directive

[1] Indicated for the treatment of inflammatory disorders
[2] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

2001/83/EC, based on pharmacovigilance data

Action: For adoption

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Dabrafenib - TAFINLAR (CAP); trametinib - MEKINIST (CAP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: To be appointed

Scope: Signal of haemophagocytic lymphohistiocytosis

Action: For adoption of PRAC recommendation

EPITT 19824 – New signal

Lead Member State(s): SE

4.1.2. Tozinameran – COMIRNATY (CAP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of histiocytic necrotizing lymphadenitis

Action: For adoption of PRAC recommendation

EPITT 19835 – New signal

Lead Member State(s): NL

4.1.3. Tozinameran – COMIRNATY (CAP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of vulval ulceration

Action: For adoption of PRAC recommendation

EPITT 19840 – New signal

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

Lead Member State(s): NL

4.1.4. Tranexamic acid (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of incorrect route of product administration

Action: For adoption of PRAC recommendation

EPITT 19844 – New signal

Lead Member State(s): IE

4.1.5. Voxelotor– OXBRYTA (CAP)

Applicant: Global Blood Therapeutics Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

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

Action: For adoption of PRAC recommendation

EPITT 19833 – New signal

Lead Member State(s): SE

4.2. New signals detected from other sources

4.2.1. Regorafenib - STIVARGA (CAP)

Applicant: Bayer Pharma AG

PRAC Rapporteur: Menno van der Elst

Scope: Signal of thrombotic microangiopathy

Action: For adoption of PRAC recommendation

EPITT 19832 – New signal

Lead Member State(s): NL

4.3. Signals follow-up and prioritisation

4.3.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/SDA/112

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of corneal graft rejection

Action: For adoption of PRAC recommendation

EPITT 19791 – Follow up to April 2022

4.3.2. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/064

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of corneal graft rejection

Action: For adoption of PRAC recommendation

EPITT 19792 – Follow-up to April 2022

4.3.3. Pneumococcal polysaccharide vaccine (23 serotypes) (NAP)

Applicant(s): various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of extensive swelling of vaccinated limb

Action: For adoption of PRAC recommendation

EPITT 19768 – Follow-up March 2022

4.3.4. Topiramate (NAP)

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of neurodevelopmental disorders due to in utero exposure

Action: For adoption of PRAC recommendation

EPITT 19825 – Follow up to July 2022

4.3.5. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/SDA/055

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of corneal graft rejection

Action: For adoption of PRAC recommendation

EPITT 19789 – Follow-up to April 2022

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0051, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.8 of the SmPC in line with the SmPC Guideline following the recommendation by PRAC in the outcome for the signal assessment of non-overt disseminated intravascular coagulation (DIC) (EPITT 19711). The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Abaloparatide - EMEA/H/C/005928

Scope: Treatment of osteoporosis

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

5.1.2. Cipaglucosidase alfa - EMEA/H/C/005703, Orphan

Applicant: Amicus Therapeutics Europe Limited

Scope: Treatment of adults aged 18 years and older with a confirmed diagnosis of Pompe disease

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

5.1.3. Melatonin - EMEA/H/C/005603

Scope: Treatment of primary insomnia

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

5.1.4. Miglustat - EMEA/H/C/005695, Orphan

Applicant: Amicus Therapeutics Europe Limited

Scope: Treatment of adults aged 18 years and older with a confirmed diagnosis of Pompe disease

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

5.1.5. Palovarotene - EMEA/H/C/004867, Orphan

Applicant: Ipsen Pharma

Scope: Treatment of fibrodysplasia ossificans progressiva

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

5.1.6. Pirfenidone - EMEA/H/C/005862

Scope: Treatment of idiopathic pulmonary fibrosis (IPF)

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

5.1.7. Sugammadex - EMEA/H/C/005935

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

5.1.8. Tabelecleucel - EMEA/H/C/004577, PRIME, Orphan

Applicant: Atara Biotherapeutics Ireland Limited, ATMP[4]

Scope: Treatment of Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV^+ PTLD)

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

5.1.9. Vadadustat - EMEA/H/C/005131

Scope: Treatment of anaemia

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. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/II/0042, Orphan

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 9.1 in order to update the 'allergy and hypersensitivity risk' from potential to identified, following reported cases of positive allergy test results, confirming the causal association between the allergies and afamelanotide

Action: For adoption of PRAC Assessment Report

5.2.2. Caspofungin - CANCIDAS (CAP) - EMEA/H/C/000379/II/0078

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jo Robays

Scope: Submission of an updated RMP version 4.1 in order to remove safety concerns and align it with the EU GVP Module V (Revision 2)

Action: For adoption of PRAC Assessment Report

[4] Advanced therapy medicinal product

5.2.3. Micafungin - MYCAMINE (CAP) - EMEA/H/C/000734/II/0047

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of Annex II and the RMP to version 23.0 to include the results of the non-interventional PASS 9463-PV-0002: effectiveness check of the prescriber checklist for Mycamine (micafungin)

Action: For adoption of PRAC Assessment Report

5.2.4. Ropeginterferon alfa-2b - BESREMI (CAP) - EMEA/H/C/004128/II/0025

Applicant: AOP Orphan Pharmaceuticals GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of an updated RMP version 1.1 for Besremi to revise safety concerns according to GVP Module V Rev.2

Action: For adoption of PRAC Assessment Report

5.2.5. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/II/0036

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 15.0) in order to reflect the outcome of a substantial amendment to a protocol previously agreed for study 156-12-299 (listed as a category 1 study): a 7.5-year, multicentre, non-interventional PASS to characterise and quantify the identified risk of idiosyncratic liver injury in Jinarc (tolvaptan) treated patients with autosomal dominant polycystic kidney disease (ADPKD) in routine clinical practice, as concluded in procedure PSA/S/0078.1 finalised in February 2021. Annex II is updated accordingly. In addition, the MAH took the opportunity to correct an oversight/editorial error in the package leaflet

Action: For adoption of PRAC Assessment Report

5.2.6. 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) post-authorisation safety study (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

Action: For adoption of PRAC Assessment Report

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

5.3.1. (1R,2S,5S)-N-((1S)-1-Cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/II/0007

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study C4671010 (listed as a category 3 study in the RMP): a phase 1, non-randomised, open label study to assess the pharmacokinetics, safety and tolerability of PF-07321332 boosted with ritonavir (Paxlovid) in adults with moderate hepatic impairment and individuals with normal hepatic function. The RMP (version 2.0) has also been submitted

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

5.3.2. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/II/0001

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.4 and 4.8 of the SmPC based on updated safety data from the Full Cumulative Pool (April 2021 data cut) from the ongoing long-term extension study B7451015. The RMP version v1.0 has also been submitted. In addition, MAH took the opportunity to implement editorial changes in the SmPC and to update the contact details of the local representatives in the package leaflet

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

5.3.3. Baloxavir marboxil - XOFLUZA (CAP) - EMEA/H/C/004974/X/0008/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Grouped variations consisting of: 1) extension application to introduce a new pharmaceutical form associated with new strength (2 mg/mL granules for oral suspension); 2) extension of indication to add a paediatric indication applicable to the new presentation, as well as to all approved presentations (EU/1/20/1500/001 and 002). The RMP (version 2.0) is updated in accordance

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

5.3.4. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0046, Orphan

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

PRAC Rapporteur: Anette Kirstine Stark

[5] Advanced therapy medicinal product

Scope: Extension of indication to include treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 5.3) are updated in accordance. In addition, the MAH took the opportunity to update the product information with minor editorial changes

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

5.3.5. Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY (CAP) - EMEA/H/C/004449/X/0040/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped application consisting of: 1) extension application to introduce a new strength 30/120/15 mg; 2) extension of indication to include a paediatric indication by adding the use in patients of 2 years of age and older and weighing at least 14 kg. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the package leaflet are updated to support the extension of indication. The RMP (version 3.1) is updated in accordance

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

5.3.6. Budesonide - JORVEZA (CAP) - EMEA/H/C/004655/II/0015, Orphan

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Update of section 4.8 of the SmPC in order to update the list of adverse drug reactions based on final results from long-term maintenance study BUL-2/EER: a double-blind, randomised, placebo-controlled, phase 3 study on the efficacy and tolerability of a 48-week treatment with two different doses of budesonide effervescent tablets vs. placebo for maintenance of clinico-pathological remission in adult patients with eosinophilic esophagitis. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. The package leaflet and RMP (version 3.0) are updated accordingly. The MAH also submitted the final report of study BUL-6/BIO: an open-label, randomised, 3-period, 3-sequence, single dose change-over trial in 18 male and female healthy volunteers, previously assessed within procedure X/0007/G concluded in March 2020

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

5.3.7. Cannabidiol - EPIDYOLEX (CAP) - EMEA/H/C/004675/II/0020, Orphan

Applicant: GW Pharma (International) B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include treatment with Epidyolex (cannabidiol) in monotherapy as adjunctive therapy of seizures associated with Lennox Gastaut syndrome (LGS) or Dravet syndrome (DS) for patients 2 years of age and older without the restriction for use only in conjunction with clobazam (CLB), based on the previously generated data in

patients treated without CLB in LGS and DS pivotal studies re-evaluated in the context of the more recent evidence from study GWEP1521: a double-blind, randomised, placebo-controlled study to investigate the efficacy and safety of cannabidiol as add-on therapy in patients with tuberous sclerosis complex (TCS) who experience inadequately-controlled seizures. As a consequence, sections 4.1, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to implement editorial changes in the product information. The RMP (version 2.1) 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/0075

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 5.1 of the SmPC in order to include updated efficacy information based on the 6 months follow-up analysis from study D8110C00001 (listed as a specific obligation in Annex II): a phase 3 randomised, double-blind, placebo-controlled, multicentre study in adults to determine the safety, efficacy and immunogenicity of Vaxzevria (COVID-19 vaccine (ChAdOx1-S [recombinant])). The RMP (version 5.1) has also been submitted. The MAH removed the important identified risk of anaphylaxis from the list of safety concerns, updated the routine and additional pharmacovigilance activities section and took the opportunity to implement other administrative updates

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

5.3.9. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[6]) - EMEA/H/W/002168/II/0015/G

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser

Scope: Grouped variations consisting of submission of four addenda from studies (listed as category 3 studies in the RMP): 1) IPM 007 (RING study): a phase 3, randomised study exploring dapivirine ring long-term safety and efficacy; 2) study MTN-015: a multisite, prospective, observational cohort study of women following human immunodeficiency virus type 1 (HIV-1) seroconversion in microbicide trials of antiretroviral (ARV)-based microbicides or oral pre-exposure prophylaxis (PrEP); 3) studies IPM 032 and MTN-025: phase 3b open-label extension (OLE) dapivirine ring trials. The data presented in the addenda are the results of retrospective next generation sequencing (NGS) and phenotype susceptibility testing on blood samples to further assess the potential development of non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance in women with unrecognized or acute HIV-1 infection. The RMP (version 0.9) is updated accordingly. Additionally, the MAH took the opportunity to update the EMA on other commitments outlined in the RMP as additional risk minimisation measures. These include the development of a healthcare

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

professional guide (HCP guide) and a user guide with agreed objectives and key messages

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

5.3.10. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/II/0009

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel, based on final results from study 17777 (ARASENS): a randomised, double-blind, placebo-controlled phase 3 study designed to demonstrate the superiority of darolutamide in combination with docetaxel over placebo in combination with docetaxel in overall survival (OS) in patients with metastatic hormone-sensitive prostate cancer (mHSPC). As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 2.1) are updated in accordance. The MAH also requested one additional year of market protection

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

5.3.11. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/II/0012

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of the final report of carcinogenicity study T104877-7 listed as a category 3 study in the RMP. This is a non-clinical study to assess the carcinogenic potential in mice. The study evaluates the effects of daily oral administration of darolutamide for a period of 6 months in tg-rasH2 transgenic mouse model. The updated RMP version 3.1 has also been submitted

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

5.3.12. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA (CAP) - EMEA/H/C/004391/II/0045

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the interim report from study GS-US-292-0106 listed as a category 3 study in the RMP. This is a Phase II/III, open-label study to evaluate of the pharmacokinetics, safety, tolerability, and antiviral activity of the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) single tablet regimen in HIV-1 infected antiretroviral treatment-naive adolescents and virologically suppressed HIV-infected children. The RMP version 8.1 has also been submitted

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

5.3.13. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/II/0053, Orphan

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Update of section 4.8 of the SmPC in order to update the list of adverse drug reactions (ADRs) following the development of an improved methodology to identify relevant ADRs likely attributable to delamanid. The package leaflet and the RMP (version 3.6) are updated accordingly

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

5.3.14. Diroximel fumarate - VUMERITY (CAP) - EMEA/H/C/005437/II/0005

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study ALK8700-A301: a phase 3 open label study to evaluate the long-term safety and tolerability of ALKS 8700 in adults with relapsing remitting multiple sclerosis (RRMS) listed as a category 3 study in the RMP. This is a multicentre, open-label study to evaluate the long-term safety, tolerability, and treatment effect over time of diroximel fumarate (DRF) administered for up to 96 weeks in adult participants with RRMS. The RMP version 1.1 has also been submitted

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

5.3.15. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/WS2323/0081; dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) -EMEA/H/C/002754/WS2323/0106; dolutegravir, rilpivirine - JULUCA (CAP) - EMEA/H/C/004427/WS2323/0045

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Nathalie Gault

Scope: Submission of the final report from study 200336 (listed as a category 3 study in the RMP): a prospective, interventional pharmacokinetic and safety study of dolutegravir (DTG)/abacavir (ABC)/lamivudine (3TC) in pregnant women. The summary of objective of this PASS study is to investigate the use of DTG during pregnancy and address the safety concerns of pregnant/breastfeeding women. The RMP versions 18.0, 20.0 and 4.0 for Tivicay, Triumeq and Juluca, respectively, have also been submitted

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

5.3.16. Dostarlimab - JEMPERLI (CAP) - EMEA/H/C/005204/II/0013

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of section 5.1 of the SmPC in order to update efficacy and safety information based on interim results from study 4010-01-001 (GARNET) listed as a specific obligation in the Annex II; This is a single-arm, open-label, phase I trial of intravenous dostarlimab in advanced solid tumors. In addition, the MAH took the opportunity to update section E of

Annex II. The RMP version 1.2 has also been submitted

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

5.3.17. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0075/G

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Grouped application consisting of line extension to add a new strain (Omicron BA.1) resulting in two new Spikevax bivalent Original/Omicron (25 µg elasomeran / 25 µg imelasomeran per dose) 0.1 mg/mL dispersion for injection presentations together with other quality variations. The SmPC, the package leaflet and labelling are updated accordingly. The RMP (version 4.2) has also been submitted.

5.3.18. Eltrombopag - REVOLADE (CAP) - EMEA/H/C/001110/II/0068

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of adult patients with primary immune thrombocytopenia (ITP) who are refractory to other treatments (e.g. corticosteroids, immunoglobulins) irrespective of time since initial diagnosis, based on an ad-hoc analysis of study TAPER (CETB115J2411): an ongoing phase 2, open-label, prospective, single-arm study in adult ITP patients who are refractory or relapsed after first-line steroids. As a consequence, sections 4.1 and 5.1 of the SmPC have been updated. In addition, the MAH took the opportunity to make some minor amendments in section 4.8 of the SmPC for increased consistency. The RMP (version 54.0) is updated accordingly

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

5.3.19. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/II/0018

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.4, 4.6 and 5.1 of the SmPC in order to update information on fertility based on interim results from studies GLPG0634-CL-227 (MANTA Ray) and GS-US-418-4279 (MANTA) listed as a category 3 study in the RMP. The package leaflet and Annex II are 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

5.3.20. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP) - EMEA/H/C/002673/WS2274/0054; REVINTY ELLIPTA (CAP) - EMEA/H/C/002745/WS2274/0052

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study HZA114971 (listed as a category 3 study

in the RMP): a multicentre randomised, double-blind, placebo-controlled, parallel-group study to evaluate the effects of a one-year regimen of orally inhaled fluticasone furoate 50 mcg once daily on growth velocity in prepubertal, paediatric subjects with asthma. The RMP version 11.1 has also been submitted

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

5.3.21. Human thrombin, human fibrinogen - TACHOSIL (CAP) - EMEA/H/C/000505/II/0117

Applicant: Corza Medical GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of children aged 1 month to 18 years, based on available bibliographical data, results from study TC-2402-040-SP which compared TachoSil with Surgicel Original as adjunct to primary surgical treatment in both adult and paediatric subjects, and results from Study TC-019-IN: a prospective, uncontrolled study in paediatric subjects. As a consequence, sections 4.1, 4.2, and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in the product information. Version 0.1 of the RMP has also been submitted

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

5.3.22. Inclisiran - LEQVIO (CAP) - EMEA/H/C/005333/II/0013

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final report from ORION-3 study (CKJX839A12201E1 or MDCO-PCS-16-01) listed as a category 3 study in the RMP. This is an open label, active comparator extension trial to assess the effect of long-term dosing of inclisiran and evolocumab given as subcutaneous injections in subjects with high cardiovascular risk and elevated LDL-C. The RMP version 2.0 has also been submitted

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

5.3.23. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2187/0098; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2187/0121

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.8 of the SmPC in alignment with the recommendations made by the CHMP to revise the pooling approach used to describe immune related adverse reactions and tabulated summaries of adverse drug reactions (ADRs) following II/0096. Individual study data included within this application has been previously reviewed by the CHMP. The updated Opdivo RMP version 29.0 and Yervoy RMP version 37.0 have also been submitted. The MAH took the opportunity to introduce editorial changes. The package leaflet was updated accordingly

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

5.3.24. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0024, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on interim results from clinical study VX17-445-105 (study 105) (listed as a category 3 study in the RMP): a phase III, open label extension study to evaluate the long-term safety and efficacy of Kaftrio (ivacaftor/tezacaftor/elexacaftor) in cystic fibrosis (CF) subjects homozygous for F508del (F/F genotype) or heterozygous for F508del and a minimal function (MF) mutation (F/MF genotypes). The RMP (version 6.1) has also been submitted. In addition, the MAH took the opportunity to implement minor corrections and editorial changes in the product information

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

5.3.25. Lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/004731/II/0005

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

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with Second-line (2L) Transplant Intended (TI) Large B-Cell Lymphoma (LBCL) for BREYANZI, based on interim analyses from pivotal study JCAR017-BCM-003: a global randomised multicentre phase III trial to compare the efficacy and safety of JCAR017 to standard of care in adult subjects with high-risk, transplant-eligible relapsed or refractory aggressive B-cell Non-Hodgkin Lymphomas (TRANSFORM). As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted

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

5.3.26. Lorlatinib - LORVIQUA (CAP) - EMEA/H/C/004646/II/0022

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Submission of an updated RMP version 5.0 to revise plans for conduct of hepatic impairment studies. The RMP is updated to reflect the termination of the hepatic impairment study B7461009: a phase 1 study to evaluate the effect of hepatic impairment on the pharmacokinetics and safety of Lorlatinib in advanced cancer patients and to include new hepatic impairment study B7461040: a phase 1, open-label, single-dose, parallel-group study to evaluate the plasma pharmacokinetics and safety of Lorlatinib in participants with moderate and severe hepatic impairment relative to participants with normal hepatic function

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

[7] Advanced therapy medicinal product

5.3.27. Lumasiran - OXLUMO (CAP) - EMEA/H/C/005040/II/0008, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Mari Thörn

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to clarify administration instructions, remove an existing warning on metabolic acidosis in patients with severe or end stage renal impairment, update the description of adverse reactions injection site reactions, abdominal pain and immunogenicity, update efficacy and pharmacokinetic information based on: 1) interim results from study ALN-GO1-005 (ILLUMINATE-C) (listed as a category 3 study in the RMP): a single arm study to evaluate efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in patients with advanced primary hyperoxaluria type 1 (PH1); 2) available long-term efficacy and safety data from ongoing studies: study ALN-GO1-003 (ILLUMINATE-A): a phase 3 randomised, double-blind, placebo-controlled study with an extended dosing period to evaluate the efficacy and safety of lumasiran in children and adults with PH1 and study ALN-GO1-004 (ILLUMINATE-B): an open-label study to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in infants and young children with primary PH1; 3) study ALN-GO1-002: a phase 2, multicentre, open-label, extension study to evaluate the long-term administration of ALN-GO1 (lumasiran) in patients with PH. The package leaflet and the RMP (version 1.1) are updated in accordance

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

5.3.28. Meningococcal group A, C, W-135 and Y conjugate vaccine - MENQUADFI (CAP) - EMEA/H/C/005084/II/0018/G

Applicant: Sanofi Pasteur

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.2, 4.5, 4.8 and 5.1 of the SmPC in order to add long term antibody persistence at least 3 years after primary vaccination, immunogenicity and safety of a booster dose of MenQuadfi in adolescents, adults, and older adults, as well as co-administration data with meningococcal serogroup B vaccine in adolescents and adults, in order to fulfil ANX/002 and ANX/003 based on final results from studies MET59 and MEQ00066, respectively, listed as specific obligations in the Annex II. MET59 is a phase 3b, open-label, partially randomised, parallel-group, active-controlled, multi-center study evaluating the immunogenicity and safety of a booster dose of an investigational quadrivalent MenACYW conjugate vaccine in adolescents and adults, while MEQ00066 is a phase 3, two-stage, randomised, open-label, multi-center trial evaluating the safety and immunogenicity of a single dose of MenACYW conjugate vaccine at least 3 years following initial vaccination with either Menomune vaccine or MenACYW conjugate vaccine in older adults. The Annex II and package leaflet are updated accordingly. The RMP version 1.1 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

5.3.29. Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/X/0039/G

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped variations consisting of: 1) extension application to introduce a new pharmaceutical form associated with new strength (8 mg/mL prolonged-release granules for oral suspension); 2) extension of indication to include treatment of neurogenic detrusor overactivity (NDO) in paediatric patients aged 3 to less than 18 years. The RMP (version 9.0) is updated accordingly

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

5.3.30. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0056

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated study design and a protocol synopsis for study CVOT-2 (listed as a category 1 study in Annex II-D (ANX/001.7)): a multicentre, randomised, double-blind, placebo-controlled phase 4 study to assess the effect of naltrexone extended release (ER)/bupropion ER on the occurrence of major adverse cardiovascular events (MACE) in overweight and obese subjects with cardiovascular disease, as requested by CHMP in the conclusions of procedure ANX 001.6 adopted in April 2021. Annex II and the RMP (version 13) are updated accordingly

Action: For adoption of PRAC Assessment Report

5.3.31. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/II/0030, Orphan

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Extension of indication to include treatment of narcolepsy with or without cataplexy in adolescents and children from the age of 6 years, based on results from Study P11-06; an ongoing phase III, double-blind, multicentre, randomised, placebo-controlled trial undertaken to evaluate safety and efficacy of pitolisant in children from 6 to less than 18 years with narcolepsy with/without cataplexy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 7.0 of the RMP has also been submitted

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

5.3.32. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - APEXXNAR (CAP) - EMEA/H/C/005451/II/0006

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.5, 4.8 and 5.1 of the SmPC based on final results from study B7471026 (listed as a category 3 study in the RMP): a phase III, randomised, double-blind trial to describe the safety and immunogenicity of 20-valent pneumococcal conjugate vaccine when coadministered with a booster dose of BNT162b2 in adults 65 years of age and older. The package leaflet and the RMP (version 2.0) were updated accordingly

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

5.3.33. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - VAXNEUVANCE (CAP) - EMEA/H/C/005477/II/0001

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of infants, children and adolescents from 6 weeks to less than 18 years of age for active immunisation for the prevention of invasive disease, pneumonia and acute otitis media for Vaxneuvance, based on final results from: 1) study V114-008: a phase 2, double-blind, randomised, multicentre trial to evaluate the safety, tolerability, and immunogenicity of V114 (pneumococcal polysaccharide conjugate vaccine (adsorbed)) compared to Prevenar 13 (pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) in healthy infants; 2) seven phase 3 studies (V114-023, V114-024, V114-025, V114-027, V114-029, V114-030, V114-031): interventional studies to evaluate the safety, tolerability and immunogenicity of V114 (pneumococcal polysaccharide conjugate vaccine (adsorbed)) in healthy and immunocompromised infants, children and adolescents. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to include editorial changes in the product information. The RMP (version 1.1) is updated accordingly

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

5.3.34. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/II/0002/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic rearranged during transfection (RET)-mutant medullary thyroid cancer for Gavreto (pralsetinib) based on the efficacy and safety data obtained from pivotal study BO42863 (ARROW): a phase 1/2 study of the highly-selective RET inhibitor, BLU-667, in patients with thyroid cancer, non-small cell lung cancer (NSCLC) and other advanced solid tumours. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. Furthermore, some minor changes to the product information have been implemented in line with the latest anticancer guidelines recommendations; 2) extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic RET fusion-positive thyroid cancer for Gavreto (pralsetinib) based on the efficacy and safety data obtained from pivotal study BO42863 (ARROW). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly

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

5.3.35. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0035/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Grouped variations consisting of: 1) extension of indication for treatment of paediatric patients (at least 4 weeks of age and weighing at least 3 kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) or other non-invasive ventilation at start of treatment based on interim results from study GS-US-540-5823: a phase 2/3 single-arm, open-label study to evaluate the safety, tolerability, pharmacokinetics and efficacy of remdesivir in participants from birth to <18 years of age with coronavirus (COVID-19); 2) extension of indication for treatment of paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19 based on data from 8 adolescent patients who were included in study GS-US-540-9012: a phase 3 randomised, double-blind placebo-controlled trial to evaluate the efficacy and safety of remdesivir treatment of COVID-19 in an outpatient setting. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 3.2) are updated accordingly

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

5.3.36. Ripretinib - QINLOCK (CAP) - EMEA/H/C/005614/II/0004, Orphan

Applicant: Deciphera Pharmaceuticals (Netherlands) B.V.

PRAC Rapporteur: Željana Margan Koletić

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in patients with hepatic impairment and update the description of pharmacokinetics based on final results from study DCC-2618-01-004: a phase 1 study of the pharmacokinetics, safety, and tolerability of ripretinib in subjects with hepatic impairment compared to healthy control subjects. The package leaflet and the RMP (version 2.0) are updated accordingly

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

5.3.37. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/X/0020/G

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped variations consisting of: 1) extension of application to introduce a new pharmaceutical form (concentrate for solution for infusion), a new strength (600 mg) and a new route of administration (intravenous use); 2) extension of application to add a new strength of 360 mg (150 mg/mL) for risankizumab solution for injection (in cartridge) for subcutaneous use. The new presentations are indicated for the treatment of patients 16 years and older with moderately to severely active Crohn’s disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy, or if such therapies are not advisable. The RMP (version 4.0) is updated in accordance

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

5.3.38. Rituximab - RIXATHON (CAP) - EMEA/H/C/003903/WS2307/0062; RIXIMYO (CAP) - EMEA/H/C/004729/WS2307/0063

Applicant: Sandoz GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of section 4.1 of the SmPC in order to include the rapid infusion regimen (90 minutes) for second and subsequent infusions in the label for patients with non-Hodgkin's lymphoma (NHL) or chronic lymphocytic leukaemia (CLL) based on non-interventional PASS CGP2013ES01R and scientific literature. The RMP version 7.0 has also been submitted

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

5.3.39. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0090

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of hidradenitis suppurativa (HS) for COSENTYX, based on interim results from two phase III studies CAIN457M2301 (SUNSHINE) and CAIN457M2302 (SUNRISE). These studies are ongoing, multi-center, randomised, double-blind, placebo-controlled, parallel group phase 3 studies conducted to assess the short (16 weeks) and long-term (up to 52 weeks) efficacy and safety of two secukinumab dose regimens (Q2W or Q4W) compared to placebo in adult subjects with moderate to severe HS. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2. of the SmPC are updated. The package leaflet and the RMP (version 11) are updated accordingly

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

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

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Marie Louise Schougaard Christiansen

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

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

5.3.41. Tenofovir alafenamide - VEMLIDY (CAP) - EMEA/H/C/004169/II/0040

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Valentina Di Giovanni

Scope: Extension of indication to include treatment of chronic hepatitis B-infected children

from 6 years and older and weighing at least 25 kilograms for Vemlidy, based on the interim results from Week 24 clinical study report (CSR) for Cohort 1 and Cohort 2 Group 1 and supporting modular summaries for the category 3 study GS-US-320-1092, 'A randomised, double-blind evaluation of the pharmacokinetics, safety, and antiviral efficacy of tenofovir alafenamide (TAF) in children and adolescent subjects with chronic hepatitis B virus infection'. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to update the wording in section 4.6 of the SmPC related to breastfeeding and pregnancies exposed to TAF, and to update the contact details of the local representative in Romania in the package leaflet. The RMP (version 8.2) is updated accordingly

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

5.3.42. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/II/0060, Orphan

Applicant: Novartis Europharm Limited, ATMP[8]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.2 of the SmPC in order to update the paediatric statement for the B-cell ALL indication and section 4.4 to update the warning on 'prior treatment with anti-CD19 therapy' as well as sections 4.4 and 4.8 in order to update safety data to reflect the pool of the 3 studies B2202, B2205J and B2001X. The proposed changes are in line with the request of the CHMP following the assessment of P46/012. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to correct the Complete Response Rate (CRR) 95% Confidence Interval (CI) on Enrolled set for E2202 study presented in Table 8 in section 5.1 of the SmPC. The RMP version 5.0 has also been submitted

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

5.3.43. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/II/0140

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Line extension to add a new strain (Omicron BA.1) resulting in a new Comirnaty bivalent Original/Omicron BA.1 (15 µg tozinameran/ 15 µg riltozinameran per dose) dispersion for injection presentation. The SmPC, the package leaflet and labelling are updated accordingly. The RMP (version 6.0) has also been submitted

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

5.3.44. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/II/0022

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include treatment of unresectable or metastatic HER2-low

[8] Advanced therapy medicinal product

(IHC 1+ or IHC 2+/ISH-) breast cancer who have received a prior systemic therapy in the metastatic setting or developed disease recurrence during or withing 6 months of completing adjuvant chemotherapy. Patients with hormone receptor positive (HR+) breast cancer must additionally have received or be ineligible for endocrine therapy; for ENHERTU, based on final results from study DS8201-A-U303 (DESTINY-Breast04). This is a phase III, multicentre, randomised, open-label, active-controlled trial of Trastuzumab Deruxtecan (T-DXd), an Anti-HER2-antibody Drug Conjugate (ADC), versus treatment of physician's choice for HER2-low, unresectable and/or metastatic breast cancer subjects. 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 the RMP (version 1.4) are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC to update the dosing recommendation for corticosteroid treatment (e.g. prednisolone) with a daily dose

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. Amifampridine - FIRDAPSE (CAP) - PSUSA/00000141/202112

Applicant: SERB SA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Avapritinib - AYVAKYT (CAP) - PSUSA/00010878/202201

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Belantamab mafodotin - BLENREP (CAP) - PSUSA/00010869/202202

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY (CAP) - PSUSA/00010695/202202

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Birch bark extract[9] - EPISALVAN[10] - PSUSA/00010446/202201

Applicant: Amryt GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.6. Brexucabtagene autoleucel - TECARTUS (CAP) - PSUSA/00010903/202201

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Bulevirtide - HEPCLUDEX (CAP) - PSUSA/00010873/202201

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Botulinum toxin type A - NUCEIVA (CAP) - PSUSA/00010796/202201

Applicant: Evolus Pharma B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Casirivimab, imdevimab - RONAPREVE (CAP) - PSUSA/00010963/202201

Applicant: Roche Registration GmbH

[9] Centrally authorised product(s) only
[10] European Commission (EC) decision on the marketing authorisation (MA) withdrawal of Episalvan dated 07 June 2022

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[11]) - EMEA/H/W/002168/PSUV/0019

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.11. Darolutamide - NUBEQA (CAP) - PSUSA/00010843/202201

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Defatted powder of Arachis hypogaea L., semen (peanuts) - PALFORZIA (CAP) - PSUSA/00010902/202201

Applicant: Aimmune Therapeutics Ireland Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Elbasvir, grazoprevir - ZEPATIER (CAP) - PSUSA/00010519/202201

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Entacapone - COMTAN (CAP); COMTESS (CAP); ENTACAPONE ORION (CAP) - PSUSA/00001223/202201

Applicant: Orion Corporation

PRAC Rapporteur: Kirsti Villikka

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

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Ertugliflozin - STEGLATRO (CAP) - PSUSA/00010682/202112

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Ertugliflozin, metformin – SEGLUROMET (CAP); ertugliflozin, sitagliptin - STEGLUJAN (CAP) - PSUSA/00010784/202112

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Fostemsavir - RUKOBIA (CAP) - PSUSA/00010911/202202

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Glucagon[12] - BAQSIMI (CAP); OGLUO (CAP) - PSUSA/00010826/202201

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

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Imipenem, cilastatin, relebactam - RECARBRIO (CAP) - PSUSA/00010830/202201

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Centrally authorised product(s) only

6.1.20. Inclisiran - LEQVIO (CAP) - PSUSA/00010904/202112

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. L-lysine hydrochloride, L-arginine hydrochloride - LYSAKARE (CAP) - PSUSA/00010786/202201

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Lonoctocog alfa - AFSTYLA (CAP) - PSUSA/00010559/202201

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Macimorelin - GHRYVELIN (CAP) - PSUSA/00010746/202201

Applicant: Consilient Health Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Metreleptin - MYALEPTA (CAP) - PSUSA/00010700/202201

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Odevixibat - BYLVAY (CAP) - PSUSA/00010949/202201

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Osilodrostat - ISTURISA (CAP) - PSUSA/00010820/202201

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Paclitaxel albumin - ABRAXANE (CAP) - PSUSA/00010123/202201

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Perflutren - LUMINITY (CAP); OPTISON (CAP) - PSUSA/00002350/202112

Applicant: GE Healthcare AS (Optison), Lantheus EU Limited (Luminity)

PRAC Rapporteur: Mari Thörn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - VAXNEUVANCE (CAP) - PSUSA/00010975/202201

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Quadrivalent influenza vaccine (recombinant, prepared in cell culture) - SUPEMTEK (CAP) - PSUSA/00010886/202201

Applicant: Sanofi Pasteur

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Ravulizumab - ULTOMIRIS (CAP) - PSUSA/00010787/202112

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Regdanvimab - REGKIRONA (CAP) - PSUSA/00010964/202202

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Valentina Di Giovanni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Remimazolam - BYFAVO (CAP) - PSUSA/00010924/202201

Applicant: PAION Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Risdiplam - EVRYSDI (CAP) - PSUSA/00010925/202202

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Romosozumab - EVENITY (CAP) - PSUSA/00010824/202201

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Salmeterol, fluticasone propionate[13] - BROPAIR SPIROMAX (CAP); SEFFALAIR SPIROMAX (CAP) - PSUSA/00010928/202201

Applicant: Teva B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[13] Centrally authorised product(s) only

6.1.37. Smallpox vaccine and monkeypox (live, modified vaccinia virus Ankara) - IMVANEX (CAP) - PSUSA/00010119/202201

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Sodium phenylbutyrate - AMMONAPS (CAP) - PSUSA/00002758/202112

Applicant: Immedica Pharma AB

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Tafasitamab - MINJUVI (CAP) - PSUSA/00010951/202201

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Tagraxofusp - ELZONRIS (CAP) - PSUSA/00010896/202201

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Umeclidinium - INCRUSE ELLIPTA (CAP); ROLUFTA ELLIPTA (CAP) - PSUSA/00010263/202112

Applicant: GlaxoSmithKline (Ireland) Limited (Incruse Ellipta), GlaxoSmithKline Trading Services Limited (Rolufta Ellipta)

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Umeclidinium bromide, vilanterol - ANORO ELLIPTA (CAP); LAVENTAIR ELLIPTA (CAP) - PSUSA/00010264/202112

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Ustekinumab - STELARA (CAP) - PSUSA/00003085/202112

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Vericiguat - VERQUVO (CAP) - PSUSA/00010950/202201

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Verteporfin - VISUDYNE (CAP) - PSUSA/00003110/202112

Applicant: CHEPLAPHARM Arzneimittel GmbH

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Vonicog alfa - VEYVONDI (CAP) - PSUSA/00010714/202112

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Ziconotide - PRIALT (CAP) - PSUSA/00003142/202112

Applicant: ESTEVE Pharmaceuticals GmbH

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. Caspofungin - CANCIDAS (CAP); NAP - PSUSA/00000576/202112

Applicant: Merck Sharp & Dohme B.V. (Cancidas), various

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Nitric oxide - INOMAX (CAP); NAP - PSUSA/00002172/202112

Applicant: Linde Healthcare AB (INOmax), various

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Paclitaxel - APEALEA (CAP); NAP - PSUSA/00002264/202112

Applicant: Inceptua AB (Apealea), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Riluzole - RILUTEK (CAP); RILUZOLE ZENTIVA (CAP); NAP - PSUSA/00002645/202112

Applicant: Sanofi Mature IP (Rilutek), Zentiva, k.s. (Riluzole Zentiva), various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Sildenafil[14] - VIAGRA (CAP); NAP - PSUSA/00002699/202112

Applicant: Upjohn EESV (Viagra), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[14] Erectile dysfunction indication only

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

6.3.1. Alitretinoin[15] (NAP) - PSUSA/00010710/202201

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Alpha amylase (NAP) PSUSA/00000104/202201

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Amino acid combinations, glucose, triglyceride combinations[16], with or without electrolytes, mineral compounds[17] [18] (NAP) - PSUSA/00010190/202112

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Amlodipine, lisinopril (NAP) - PSUSA/00010192/202112

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Anthrax vaccine (NAP) - PSUSA/00010771/202112

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[15] Oral use only
[16] E.g. olive oil, soya bean oil, fish oil
[17] Intravenous (I.V.) application only
[18] Nationally authorised product Numeta only

6.3.6. Beclometasone (NAP) - PSUSA/00000306/202112

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Beclomethasone, salbutamol (NAP) - PSUSA/00000309/202201

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Bendamustine hydrochloride (NAP) - PSUSA/00003162/202201

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Betula verrucosa[19] [20] (NAP) - PSUSA/00010815/202201

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Botulinum neurotoxin type A (150 kD) free from complexing proteins (NAP) - PSUSA/00009084/202112

Applicant(s): various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Botulinum toxin A (NAP) - PSUSA/00000426/202112

Applicant(s): various

[19] Allergen for therapy
[20] Sublingual tablet(s) only

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Botulinum toxin A-haemagglutinin complex (NAP) - PSUSA/00000427/202112

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Bupropion (NAP) – PSUSA/00000461/202112

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Camellia sinensis, leaf, dry extract refined[21] [22](NAP) - PSUSA/00010569/202112

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Cefotaxime (NAP) - PSUSA/00000599/202112

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Ciclosporin[23] (NAP) - PSUSA/00000745/202112

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[21] Derived from Camellia sinensis, L.O.KUNTZE
[22] Topical use only
[23] For systemic use only

6.3.17. Citalopram (NAP) - PSUSA/00000779/202112

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Dexlansoprazole, lansoprazole (NAP) - PSUSA/00001827/202112

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Dexketoprofen, tramadol (NAP) - PSUSA/00010468/202201

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Escitalopram (NAP) - PSUSA/00001265/202112

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Flumazenil (NAP) - PSUSA/00001413/202112

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Flunitrazepam (NAP) - PSUSA/00001418/202201

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Levobunolol[24] (NAP) - PSUSA/00010109/202201

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Methohexital (NAP) - PSUSA/00010656/202201

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Niflumic acid (NAP) - PSUSA/00002157/202112

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Octenidine dihydrochloride, phenoxyethanol (NAP) - PSUSA/00002199/202201

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Roxithromycin (NAP) - PSUSA/00002669/202112

Applicant(s): various

PRAC Lead: Valentina Di Giovanni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[24] Ophthalmic indication only

6.3.28. Terbutaline (NAP) - PSUSA/00002897/202112

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Testosterone[25] (NAP) - PSUSA/00010631/202112

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Testosterone[26] (NAP) - PSUSA/00002908/202112

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.31. Topiramate (NAP) - PSUSA/00002996/202201

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.32. Typhoid vaccine (live, attenuated) - PSUSA/00003067/202112

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.33. Valaciclovir (NAP) - PSUSA/00003086/202112

Applicant(s): various

PRAC Lead: Jana Lukačišinová

[25] For all formulations (apart from topical use)
[26] Topical use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/LEG 053.8

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Cumulative review of the impact of immunogenicity testing on the safety and efficacy of the product in line with the conclusions of the PSUR single assessment (PSUSA) procedure for algluclosidase alfa (PSUSA/00000086/202109) adopted in June 2022

Action: For adoption of advice to CHMP

6.4.2. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/LEG 015.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 010 [submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure] as per the request for supplementary information (RSI) adopted in February 2022

Action: For adoption of advice to CHMP

6.4.3. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/LEG 010.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 010 [submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure] as per the request for supplementary information (RSI) adopted in February 2022

Action: For adoption of advice to CHMP

6.4.4. Dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/LEG 005.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: David Olsen

Scope: MAH's response to LEG 010 [Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure] as per the request for supplementary information (RSI) adopted in February 2022

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/II/0141

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the occurrence of myocarditis because more information is available in the age group 5-11 years; and to update the statement in the SmPC section 4.4 regarding the risk of myocarditis after a third dose of Comirnaty based on real-world evidence requested by PRAC following the assessment of MEA/002.13 procedure concluded in June 2022. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in section 4.4 of the SmPC

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

6.5.2. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/WS2268/0079; dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/WS2268/0104; dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/WS2268/0031; dolutegravir, rilpivirine - JULUCA (CAP) - EMEA/H/C/004427/WS2268/0044

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to add 'weight increased' with a frequency common based on available data/results from study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the post-authorisation measures (LEG procedures) adopted in February 2022 that followed a request adopted in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) finalised in September 2021. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a minor editorial change in the German SmPC for Juluca (dolutegravir/rilpivirine)

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[27]

6.6.1. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 014.5

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Sixth expedited summary safety report (SSR) for Nuvaxovid (COVID-19 vaccine (recombinant, adjuvanted)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[28]

7.1.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/PSA/S/0088

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Substantial amendment to a non-interventional post-authorisation safety study to investigate drug utilisation and safety monitoring patterns for Lemtrada (alemtuzumab)

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

7.1.2. Belimumab - BENLYSTA (CAP) - EMEA/H/C/PSA/S/0085

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: A 5-Year prospective observational registry to assess adverse events of interest and effectiveness in adults with active, autoantibody-positive systemic lupus erythematosus treated with or without belimumab

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

7.1.3. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/PSA/S/0084

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: An observational study of blinatumomab safety and effectiveness, utilisation, and treatment practices to characterise the safety of Blincyto in routine clinical practice. Blincyto

[27] 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

[28] In accordance with Article 107n of Directive 2001/83/EC

efficacy, medication errors, and utilisation and select healthcare resource use while using Blincyto will also be described. Safety and efficacy of Blincyto in specified subgroups of patients will also be assessed

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

7.1.4. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/PSP/S/0099

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Jo Robays

Scope: A long-term follow-up study for participants previously treated with ciltacabtagene autoleucel to collect data on delayed adverse events after administration of cilta-cel, and to characterize and understand the long-term safety profile of cilta-cel

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

7.1.5. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/PSP/S/0093.3

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/0093.2 [an observational registry to provide data on long-term safety of fenfluramine in routine practice, with a focus on characterising and quantifying the important potential risks VHD and PAH (primary objective), and growth retardation (secondary objective). In addition, data on the frequency of echocardiographic monitoring will contribute to assess the effectiveness of risk minimisation measures]

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

7.1.6. Methylphenidate hydrochloride (NAP) - EMEA/H/N/PSA/S/0074.1

Applicant: MEDICE Arzneimittel Pütter GmbH & Co. KG

PRAC Rapporteur: Martin Huber

Scope: Interim study report for a protocol previously agreed in September 2021 (PSA/S/0074): a multicentre, observational, prospective PASS to evaluate the safety concerns of long-term cardiovascular and psychiatric risks within the adult attention deficit/hyperactivity disorder (ADHD) population taking Medikinet Retard (methylphenidate hydrochloride) according to normal standard clinical practice

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[29]

7.2.1. (1R,2S,5S)-N-((1S)-1-Cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-

[29] 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

azabicyclo[3.1.0]hexane-2-carboxamide, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/MEA 009

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Protocol for study C4671037: use and safety of Paxlovid during pregnancy and among patients with moderate or severe hepatic or renal impairment

Action: For adoption of advice to CHMP

7.2.2. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 002

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study B7451084: an active surveillance study to monitor the real-world safety of abrocitinib among patients with atopic dermatitis (AD) in the EU. The objective of the study is to estimate the incidence rates of safety endpoints of interest among AD patients receiving abrocitinib and AD patients receiving appropriate systemic treatments including dupilumab for AD in a real-world setting

Action: For adoption of advice to CHMP

7.2.3. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 003

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study B7451085: a drug utilisation study to evaluate the effectiveness of risk minimisation measures (RMMs) for abrocitinib in the EU using electronic healthcare data. The study objectives will be to evaluate indicators of HCP's adherence to the risk minimisation measures in accordance with the abrocitinib SmPC and prescriber brochure

Action: For adoption of advice to CHMP

7.2.4. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 004

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study B7451015: an adolescent imaging substudy to evaluate if abrocitinib has any clinically meaningful effects on bone growth and development

Action: For adoption of advice to CHMP

7.2.5. Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/MEA 005.3

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 005.2 [protocol for study KT-EU-472-5966: a prescriber

survey to assess prescribers' understanding of the risks of Tecartus (KTE-X19) to evaluate the effectiveness of risk minimisation activities, namely healthcare professional (HCP) educational materials and patient alert card (PAC) [final study report expected in September 2023] (from initial opinion/marketing authorisation(s) (MA))] as per the request for supplementary information (RSI) adopted in May 2022

Action: For adoption of advice to CHMP

7.2.6. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/MEA 011.2

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: MAH's response to MEA 011.1 [protocol for study AMY2009: a multicentre, prospective study of daratumumab-based therapy in newly diagnosed patients with light-chain (AL) amyloidosis (from variation II/0043)] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.2.7. Diroximel fumarate - VUMERITY (CAP) - EMEA/H/C/005437/MEA 001.1

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response MEA 001 [protocol for study 272MS401: Vumerity (diroximel fumarate) prospective multiple sclerosis (MS) pregnancy exposure registry] as per the request for supplementary information (RSI) adopted in April 2022

Action: For adoption of advice to CHMP

7.2.8. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 034.4

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: MAH's response 034.2 [protocol for a study monitoring the safety of Spikevax (COVID-19 vaccine) in pregnancy: an observational study using routinely collected health data in five European countries] as per the request for supplementary information (RSI) adopted in April 2022 together with a statistical analysis plan (SAP)

Action: For adoption of advice to CHMP

7.2.9. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 005.3

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response MEA 005.2 [protocol for study ZX008-2102: a drug utilisation study (DUS) in Europe to describe fenfluramine use in routine clinical practice [final report expected in August 2025] (from initial opinion/marketing authorisation)] as per the request

for supplementary information (RSI) adopted in April 2022

Action: For adoption of advice to CHMP

7.2.10. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/MEA 046.5

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Substantial amendment (version 5.0) to a protocol previously endorsed in November 2017 for study CC-5013-MCL-005 to further investigate and characterise the association of lenalidomide and tumour flare reaction (TFR)/high tumour burden following the extension of indication for the treatment of adult patients with relapsed and/or refractory mantle cell lymphoma (RRMCL)

Action: For adoption of advice to CHMP

7.2.11. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/MEA 015.1

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 015 [protocol for study 218065: a PASS to describe real-world safety and effectiveness of mepolizumab in paediatric eosinophilic granulomatosis with polyangiitis (EGPA) patients in Europe] as per the request for supplementary information (RSI) adopted in May 2022

Action: For adoption of advice to CHMP

7.2.12. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.13

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the 4th feasibility report and final study protocol for PASS NB-451: an observational retrospective drug utilisation study (DUS) of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) in Europe and the United States to describe the demographic and baseline characteristics of users of Mysimba (naltrexone hydrochloride/bupropion hydrochloride), evaluate patterns of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) initiation and use)

Action: For adoption of advice to CHMP

7.2.13. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 005

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Protocol for study IM0471037: a post-authorisation safety study (PASS) titled "Long-term real-world safety of ozanimod – A post-authorisation safety study (PASS) in patients

diagnosed with ulcerative colitis". This study is a category 3 study (required additional pharmacovigilance activity - UC indication) listed in the RMP version 3.0

Action: For adoption of advice to CHMP

7.2.14. Pegcetacoplan - ASPAVELI (CAP) - EMEA/H/C/005553/MEA 002

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Protocol for study Sobi.PEGCET-301: a PASS using registry data for pegcetacoplan to evaluate the occurrence of serious infections in patients with paroxysmal nocturnal hemoglobinuria (PNH) treated with pegcetacoplan

Action: For adoption of advice to CHMP

7.2.15. Pegcetacoplan - ASPAVELI (CAP) - EMEA/H/C/005553/MEA 003

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Protocol for study Sobi.PEGCET-302: a post-authorisation safety study for assessment of pregnancy outcomes in patients with paroxysmal nocturnal hemoglobinuria (PNH) exposed to pegcetacoplan during pregnancy

Action: For adoption of advice to CHMP

7.2.16. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 001

Applicant: Biohaven Pharmaceutical Ireland DAC

PRAC Rapporteur: Anette Kirstine Stark

Scope: Protocol for study BHV3000-402: rimegepant pregnancy registry study together with a statistical analysis plan (SAP)

Action: For adoption of advice to CHMP

7.2.17. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 002

Applicant: Biohaven Pharmaceutical Ireland DAC

PRAC Rapporteur: Anette Kirstine Stark

Scope: Protocol for study BHV3000-403: a rimegepant pregnancy outcomes study together with a statistical analysis plan (SAP)

Action: For adoption of advice to CHMP

7.2.18. Tebentafusp - KIMMTRAK (CAP) - EMEA/H/C/004929/MEA 002

Applicant: Immunocore Ireland Limited

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for a physician's survey to evaluate the effectiveness of additional risk minimisation measure for (educational materials) cytokine release syndrome (CRS) associated with Kimmtrak administration

Action: For adoption of advice to CHMP

7.2.19. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 017.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 017.1 [protocol for study A3921352: an active surveillance, post-authorisation study to characterise the safety of tofacitinib in patients with moderately to severely active ulcerative colitis in the real-world setting using data from the united registries for clinical assessment and research (UR-CARE) in the European Union (EU)] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.2.20. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 012.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 012 [protocol for study P21-825: an evaluation of the effectiveness of additional risk minimisation measures for upadacitinib in the treatment of atopic dermatitis] as per request for supplementary information (RSI) adopted in February 2022

Action: For adoption of advice to CHMP

7.2.21. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 014.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 014 [protocol for study P21-824: a study of growth and development in adolescents with atopic dermatitis who receive upadacitinib] as per request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.2.22. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 015

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Protocol for study P22-907 (listed as category 3 study in the RMP): a one-time, cross-sectional survey study evaluating the effectiveness of the DHPC and of the revised venetoclax SmPC among hematologists in select European countries

Action: For adoption of advice to CHMP

7.2.23. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 016

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Protocol for study P22-905 (listed as category 3 study in the RMP): a one-time, cross-sectional survey study to evaluate effectiveness of the patient card among adult patients recently treated with venetoclax for CLL per usual care in select European countries

Action: For adoption of advice to CHMP

7.2.24. Zanamivir - DECTOVA (CAP) - EMEA/H/C/004102/MEA 003.1

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 003 [protocol for study 208140: an intravenous (IV) zanamivir pregnancy registry to evaluate pregnancy outcomes among women exposed to IV zanamivir at any time during pregnancy (from initial marketing authorisation/opinion)]

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[30]

7.3.1. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/PSR/S/0027

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Final study report comprising the pharmacoepidemiological study program of rivaroxaban use and potential adverse outcomes in routine clinical practice in the UK, Germany, the Netherlands and Sweden

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[31]

7.4.1. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/II/0027

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to update information based on final results from study ML39302 listed as a category 3 study in the RMP in order to fulfil MEA/003.5; this is a non-interventional PASS study to investigate the effectiveness, safety and utilisation of cobimetinib and vemurafenib in patients with and without brain metastasis

[30] In accordance with Article 107p-q of Directive 2001/83/EC
[31] 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

with BRAF V600 mutant melanoma under real world conditions. The RMP version 5.0 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.2. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0038

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study MS1222-0003 (listed as a category 3 study in the RMP) as assessment of anti-platelet factor 4 (PF4) antibodies prior to, and following, vaccination with AZD1222: a study where sera of vaccinated individuals in study D8110C00001 are tested to elucidate whether vaccination with Vaxzevria (COVID-19 vaccine) leads to increased levels of circulating anti-PF4 antibodies, a key component of the hypothesised mechanism underlying thrombosis with thrombocytopenia syndrome (TTS)

Action: For adoption of PRAC Assessment Report

7.4.3. Flutemetamol (^{18}F) - VIZAMYL (CAP) - EMEA/H/C/002557/II/0029

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study GE067-027 (listed as a category 3 study in the RMP): a non-interventional PASS to evaluate the effectiveness of Vizamyl (flutemetamol (^{18}F)) reader training in Europe. The submission also includes a comprehensive root-cause analysis on the contributing factors having an impact on reader performance as requested by PRAC. The RMP (version 3.1) is updated accordingly and includes relevant updates to reflect the completion of study GE067-028 on the use pattern of Vizamyl (flutemetamol (^{18}F)) in post-authorisation setting in the EU, as previously assessed in MEA 003.3

Action: For adoption of PRAC Assessment Report

7.4.4. Loxapine - ADASUVE (CAP) - EMEA/H/C/002400/II/0033

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update safety information on bronchospasm based on final results from study AMDC-204-401 EU PASS (listed as a category 3 study in the RMP): a post-authorisation observational study to evaluate the safety of Adasuve (loxapine for inhalation) in agitated persons in routine clinical care (assessed in variation II/0032 finalised in May 2021). The package leaflet and labelling are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

Action: For adoption of PRAC Assessment Report

7.4.5. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/II/0083

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final report from study 20070797 (listed as a category 3 study in the RMP): an observational study assessing the long-term safety of romiplostim treatment in real-life clinical practice in three Nordic countries. The RMP (version 21.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/II/0081, Orphan

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 5.1 of the SmPC in order to update information based on final results from study B3461029 listed as a Specific Obligation in the Annex II of the Product Information. This is a non-interventional PASS sub-study evaluating effects of tafamidis on disease progression in patients with non-Val30Met mutations and symptomatic neuropathy. Consequently, the MAH proposes a switch from marketing authorisation under exceptional circumstances to full marketing authorisation given the fulfilment of the SOB. The Annex II and package leaflet are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

Action: For adoption of PRAC Assessment Report

7.4.7. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0056

Applicant: Amgen Europe B.V., ATMP[32]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study 20120139 (listed as a category 3 study in the RMP): is a multicenter, observational registry study to evaluate the survival and long-term safety of subjects who previously received talimogene laherparepvec in Amgen or BioVEX sponsored clinical trials [in fulfilment of MEA/004]

Action: For adoption of PRAC Assessment Report

7.4.8. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0095

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final report from study PSOLAR (C0168Z03) (listed as a category 3 study in the RMP): a multicenter, open registry of patients with psoriasis who are candidates for sistemic therapy including biologics: PSOLAR. The RMP (version 22.2) is updated accordingly

[32] Advanced therapy medicinal product

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. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 024.17

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: MAH's response to MEA 024.16 [annual report (covering period from 04 July 2020 to 02 July 2021) on adverse events and/or lack of efficacy, immunological data, follow-up growth disturbances in children and data on urinary hexose tetrasaccharide (Hex4) from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.5.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 025.17

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: MAH's response to MEA 025.16 [annual report (covering period from 04 July 2020 to 02 July 2021) on data on patients with renal or hepatic insufficiency from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.5.3. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 008.2

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Third yearly report for study CC 10004 PSA-012: evaluation of the long-term safety and safety outcomes for psoriatic arthritis patients treated with Otezla (apremilast) in the British Society for Rheumatology Psoriatic Arthritis Register (BSRBR-PsA) [final clinical study report (CSR) expected in Q2 2026]

Action: For adoption of advice to CHMP

7.5.4. Beclometasone, formoterol, glycopyrronium bromide - TRIMBOW (CAP) - EMEA/H/C/004257/MEA 002.2

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: First progress report for study CLI-05993BA1-05 (TRIBE): a multinational database cohort study to assess adverse cardiovascular and cerebrovascular outcomes in patients with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurised metered dose inhaler (pMDI) and MAH's response to MEA 002.1 as per the request for supplementary information (RSI) adopted in December 2021

Action: For adoption of advice to CHMP

7.5.5. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 007.5

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 007.3 and MEA 007.4 [amendment to a protocol previously agreed in November 2017 for study 109MS401 (ESTEEM): a multicentre, global, observational study to collect information on safety and to document the drug utilisation of Tecfidera (dimethyl fumarate) when used in routine medical practice in the treatment of relapsing multiple sclerosis] as per the request for supplementary information (RSI) adopted in April 2021, together with the seventh annual progress report for the study

Action: For adoption of advice to CHMP

7.5.6. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 012.11

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Eleventh annual interim report for study D2404: a multinational pregnancy exposure registry in patients with multiple sclerosis (MS) taking Gilenya (fingolimod) from the pregnancy intensive monitoring programme (PRIM)

Action: For adoption of advice to CHMP

7.5.7. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA 004.13

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual report for the passive enhanced safety surveillance (ESS) D2560C00008: a post-marketing non-interventional cohort study of the safety of live attenuated influenza vaccine (LAIV) in subjects 2 through 17 years of age for the 2021-2022 influenza season

Action: For adoption of advice to CHMP

7.5.8. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/MEA 036.4

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the progress report for study CA184557: Long-term follow-up of ipilimumab treated paediatric patients enrolled in the Dutch melanoma treatment registry (DMTR)

Action: For adoption of advice to CHMP

7.5.9. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.11

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Fifth 6-monthly progress report for study A-LUT-T-E02-402 (SALUS): an international, non-interventional, post-authorisation long-term safety study of Lutathera (lutetium (177Lu) oxodotreotide) in patients with unresectable or metastatic, well-differentiated, somatostatin receptor positive, gastro-enteropancreatic neuroendocrine tumours together with MAH's response to MEA 001.9 as pr the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.5.10. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 005.4

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual interim report 2021 for epidemiological study 15689: an evaluation of adverse events of special interest (AESI) in the European PEDiatric NETwork (PedNet) for haemophilia management registry

Action: For adoption of advice to CHMP

7.5.11. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 002.9

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final results for the validation sub study to assess the positive predictive value of the identification of specific primary safety events of interest (angioedema, acute pancreatitis, hepatotoxicity, and myotoxicity) for the post-authorisation multi-database safety LCZ696B2014: a non-interventional, post-authorisation, multi-database safety study to characterize the risk of angioedema and other specific safety events of interest in association with initiation of Entresto (sacubitril/valsartan) or use of an ACE inhibitor in adult patients with heart failure (HF)

Action: For adoption of advice to CHMP

7.5.12. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 004.12

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final results for the validation sub study to assess the positive predictive value of the identification of specific primary safety events of interest (angioedema, acute pancreatitis, hepatotoxicity, and myotoxicity) for the post-authorisation multi-database safety study LCZ696B2015: a non-interventional, post-authorisation, multi-database safety study, using a case-control design, to assess the risk of myotoxicity, hepatotoxicity, and acute pancreatitis in statin-exposed HF patients with or without concomitant use of sacubitril/valsartan (Entresto)

Action: For adoption of advice to CHMP

7.5.13. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/MEA 002.6

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final results for the validation sub study to assess the positive predictive value of the identification of specific primary safety events of interest (angioedema, acute pancreatitis, hepatotoxicity, and myotoxicity) for the post-authorisation multi-database safety LCZ696B2014: a non-interventional, post-authorisation, multi-database safety study to characterize the risk of angioedema and other specific safety events of interest in association with initiation of Entresto (sacubitril/valsartan) or use of an ACE inhibitor in adult patients with heart failure (HF)

Action: For adoption of advice to CHMP

7.5.14. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/MEA 003.9

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final results for the validation sub study to assess the positive predictive value of the identification of specific primary safety events of interest (angioedema, acute pancreatitis, hepatotoxicity, and myotoxicity) for the post-authorisation multi-database safety study LCZ696B2015: a non-interventional, post-authorisation, multi-database safety study, using a case-control design, to assess the risk of myotoxicity, hepatotoxicity, and acute pancreatitis in statin-exposed HF patients with or without concomitant use of sacubitril/valsartan (Entresto)

Action: For adoption of advice to CHMP

7.5.15. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/MEA 002.3

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

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

Action: For adoption of advice to CHMP

7.5.16. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 045.9

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Third annual progress report for study RRA-20745: an observational PASS to describe the safety of ustekinumab and other Crohn's disease treatments in a cohort of patients with Crohn's disease

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/MEA 002.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: MAH's response to MEA 002.3 [interim report for study D8220C00008 (ASSURE): a phase 3b, multicentre, open-label, single-arm study of acalabrutinib (ACP-196) in subjects with chronic lymphocytic leukaemia to address missing information around moderate to severe cardiac impaired patients] as per request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.6.2. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/SOB 008

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of statistical analysis plan (SAP) for study NO BLU-285-1406: an imposed non-interventional PASS aiming to collect long-term safety and efficacy data for avapritinib in first-line patients with PDGFRA D842V-mutated gastrointestinal stromal tumour (GIST) given as specific obligation 3 (SOB3) of the conditional marketing authorisation for AYVAKYT

Action: For adoption of advice to CHMP

7.6.3. Cabazitaxel - CABAZITAXEL ACCORD (CAP) - EMEA/H/C/005178/MEA 001.2

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Third six-monthly review of cases of 'medication error' for cabazitaxel reported during routine signal management activities

Action: For adoption of advice to CHMP

7.6.4. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 006.6

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 006.3 [statistical analysis plan (SAP) for study COVID-19 vaccines International Pregnancy Exposure Registry (C-VIPER) (listed as a category 3 study in the RMP): a pregnancy registry of women exposed to Vaxzevria (AZD1222 – COVID-19 vaccine) immediately before or during pregnancy (from initial opinion/marketing authorisation(s) (MA))] as per request for supplementary information (RSI) adopted in April 2022

Action: For adoption of advice to CHMP

7.6.5. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 004.7

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: MAH's response to MEA 004.5 [submission of a statistical analysis plan (SAP) for study mRNA-1273-P904 (study 1) (listed as a category 3 study in the RMP): a post-authorisation active surveillance safety study using secondary data to monitor real-world safety of Spikevax (COVID-19 mRNA-1273 vaccine) in Europe - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals in European populations and electronic database assessment of use in pregnant women [final clinical study report (CSR) expected in December 2023]] as per request for supplementary information adopted in April 2022

Action: For adoption of advice to CHMP

7.6.6. Icatibant - FIRAZYR (CAP) - EMEA/H/C/000899/MEA 034.1

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Mari Thörn

Scope: MAH's response to MEA 034 [proposal for discontinuation of icatibant outcome survey (IOS): a prospective, international, observational open-ended disease registry designed to document over time the routine clinical outcomes of adult and paediatric patients with hereditary angioedema (HAE; HAE types I and II and HAE with normal C1-esterase inhibitor), angiotensin converting enzyme inhibitor (ACE-I)-induced angioedema, non-histaminergic idiopathic angioedema, and acquired angioedema; and notification of change to the legal entity sponsoring the study] as per request for supplementary information (RSI) adopted in April 2022

Action: For adoption of advice to CHMP

7.6.7. Melatonin - SLENYTO (CAP) - EMEA/H/C/004425/REC 002.2

Applicant: RAD Neurim Pharmaceuticals EEC SARL

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Third annual French 'recommendation temporaire d'utilisation (RTU)' report on special temporary recommendation of use for Circadin (melatonin) 2-6 mg in the autism spectrum disorder (ASD) and neurogenetic 6-18 year-old population for the period from October 2015 to July 2019

Action: For adoption of advice to CHMP

7.6.8. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/MEA 002.1

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002 [protocol for study LTE1 (listed as a category 3 study in the RMP): a phase 3, open-label study to evaluate the long-term safety and efficacy of zanubrutinib, as monotherapy or in combination, in patients with B-cell malignancies who are or were previously enrolled in a BeiGene parent study and who are still benefiting or may benefit from treatment with zanubrutinib, or who are willing to have long-term survival follow-up] as adopted in May 2022

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Evinacumab - EVKEEZA (CAP) - EMEA/H/C/005449/S/0005 (without RMP)

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thörn

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/S/0099 (without RMP)

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Liana Gross-Martirosyan

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. Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/R/0025 (without RMP)

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/R/0020 (without RMP)

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/R/0074 (without RMP)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Sotorasib - LUMYKRAS (CAP) - EMEA/H/C/005522/R/0002 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.5. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/R/0137 (without RMP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.6. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/R/0023 (without RMP)

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Anagrelide - ANAGRELIDE MYLAN (CAP) - EMEA/H/C/004585/R/0010 (without RMP)

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Darunavir - DARUNAVIR KRKA (CAP) - EMEA/H/C/004273/R/0013 (without RMP)

Applicant: KRKA, d.d., Novo mesto

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Darvadstrocel - ALOFISEL (CAP) - EMEA/H/C/004258/R/0036 (with RMP)

Applicant: Takeda Pharma A/S, ATMP[33]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

[33] Advanced therapy medicinal product

8.3.4. Efavirenz, emtricitabine, tenofovir disoproxil – EFAVIRENZ, EMTRICITABINE, TENOFOVIR DISOPROXIL KRKA (CAP) - EMEA/H/C/004274/R/0015 (without RMP)

Applicant: KRKA, d.d., Novo mesto

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/R/0015 (without RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/R/0015 (without RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - EMEA/H/C/004313/R/0018 (without RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Fulvestrant - FULVESTRANT MYLAN (CAP) - EMEA/H/C/004649/R/0016 (without RMP)

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Hydrocortisone - ALKINDI (CAP) - EMEA/H/C/004416/R/0014 (without RMP)

Applicant: Diurnal Europe BV

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Gemtuzumab ozogamicin - MYLOTARG (CAP) - EMEA/H/C/004204/R/0025 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0034 (without RMP)

Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Rurioctocog alfa pegol - ADYNOVI (CAP) - EMEA/H/C/004195/R/0033 (with RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Trastuzumab - HERZUMA (CAP) - EMEA/H/C/002575/R/0050 (with RMP)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Ranibizumab - LUCENTIS (CAP) – EMEA/H/C/000715/II/0098

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: PRAC consultation on a variation to update section 4.6 of the SmPC regarding breastfeeding as requested in the conclusions of the PSUSA procedure (PSUSA/00002609/202010) adopted by PRAC in May 2021, based on a cumulative assessment of pre-clinical studies, pharmacokinetic data, published literature and post-marketing spontaneous reports. The package leaflet is updated accordingly

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. Vote by proxy

None

12.1.3. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q2 2022

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2022 - update

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q2 2022 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q2 2022

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

None

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. Coronavirus (COVID-19) pandemic - coreRMP19: update

PRAC lead: Jean-Michel Dogné, Brigitte Keller-Stanislawski, Zane Neikena, Marie Louise Schougaard Christiansen, Anette Kirstine Stark, Menno van der Elst, Ulla Wändel Liminga

Action: For adoption

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.15.3. Good pharmacovigilance practices (GVP) module VIII on 'Post-authorisation safety studies (PASS)' – Revision

Action: For discussion

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. EMA Scientific Committees support – organisational adjustments

Action: For discussion

13. Any other business

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/