08 February 2021
EMA/PRAC/80497/2021
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 08-11 February 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

08 February 2021, 10:30 – 19:30, via teleconference

09 February 2021, 08:30 – 19:30, via teleconference

10 February 2021, 08:30 – 19:30, via teleconference

11 February 2021, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

25 February 2021, 09:00 – 12:00, via teleconference

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 08-11 February 2021. See February 2021 PRAC minutes (to be published post March 2021 PRAC meeting).

1.2. Agenda of the meeting on 08-11 February 2021

Action: For adoption

1.3. Minutes of the previous meeting on 11-14 January 2021

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

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

Action: For adoption of a list of questions (LoQ)

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Olanzapine – OLANZAPINE APOTEX (CAP); OLANZAPINE GLENMARK (CAP); OLANZAPINE GLENMARK EUROPE (CAP); OLANZAPINE MYLAN (CAP); OLANZAPINE TEVA (CAP); OLAZAX (CAP); OLAZAX DISPERZI (CAP); ZALASTA (CAP); ZYPADHERA (CAP); ZYPREXA (CAP); ZYPREXA VELOTAB (CAP); NAP

Applicant(s): Apotex Europe BV (Olanzapine Apotex), Eli Lilly Nederland B.V. (Zypadhera, Zyprexa, Zyprexa Veotab), Glenmark Arzneimittel GmbH (Olanzapine Glenmark, Olanzapine Glenmark Europe), Glenmark Pharmaceuticals (Olazax, Olazax Disperzi), Krka, d.d., Novo mesto (Zalasta), Mylan S.A.S (Olanzapine Mylan); Teva B.V.

PRAC Rapporteur: To be appointed

Scope: Signal of cardiomyopathy

Action: For adoption of PRAC recommendation

EPITT 19663 – New signal

Lead Member State(s): FI

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

4.1.2. Olaparib – LYNPARZA (CAP)

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of Pneumocystis jirovecii pneumonia

Action: For adoption of PRAC recommendation

EPITT 19651 – New signal

Lead Member State(s): IT

4.1.3. Remdesivir – VEKLURY (CAP)

Applicant(s): Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Signal of sinus bradycardia

Action: For adoption of PRAC recommendation

EPITT 19659 – New signal

Lead Member State(s): CZ

4.1.4. Romosozumab – EVENITY (CAP)

Applicant(s): UCB Pharma S.A.

PRAC Rapporteur: Adrien Inoubli

Scope: Signal of renal impairment

Action: For adoption of PRAC recommendation

EPITT 19648 – New signal

Lead Member State(s): FR

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Ceftriaxone (NAP)

Applicant(s): various

PRAC Rapporteur: Zane Neikena

Scope: Signal of hepatitis

Action: For adoption of PRAC recommendation

EPITT 19603 – Follow-up to September 2020

4.3.2. Filgrastim – ACCOFIL (CAP), FILGRASTIM HEXAL (CAP), GRASTOFIL (CAP), NIVESTIM (CAP), RATIOGRASTIM (CAP), TEVAGRASTIM (CAP), ZARZIO (CAP); NAP

Applicant(s): Accord Healthcare S.L.U. (Accofil, Grastofil), AbZ Pharma GmbH (Biograstim), Pfizer Europe MA EEIG (Nivestim), Ratiopharm GmbH (Ratiograstim), Sandoz GmbH (Zarzio), Teva GmbH (Tevagrastim)

PRAC Rapporteur: Kirsti Villikka

Scope: Signal of immune reconstitution inflammatory syndrome (IRIS)

Action: For adoption of PRAC recommendation

EPITT 19587 – Follow-up to September 2020

4.3.3. 3-hydroxy 3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins): atorvastatin (NAP); fluvastatin (NAP); lovastatin (NAP); pitavastatin (NAP); pravastatin (NAP); rosuvastatin (NAP); simvastatin (NAP)

Applicant(s): various

PRAC Rapporteur: Adrien Inoubli

Scope: Signal of bullous pemphigoid

Action: For adoption of PRAC recommendation

EPITT 19586 – Follow-up to September 2020

4.3.4. Prednisolone (NAP); prednisone (NAP)

Applicant(s): various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of bradycardia

Action: For adoption of PRAC recommendation

EPITT 19613 – Follow-up to October 2020

4.3.5. Remdesivir - VEKLURY (CAP)

Applicant(s): Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Signal of acute kidney injury

Action: For adoption of PRAC recommendation

EPITT 19605 – Follow-up to October 2020

4.4. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Abiraterone acetate - EMEA/H/C/005649

Scope: Treatment of prostate cancer in adult men

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

5.1.2. Abiraterone acetate - EMEA/H/C/005368

Scope: Treatment of metastatic castration resistant prostate cancer

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

5.1.3. Azacitidine - EMEA/H/C/004761

Scope: Treatment for acute myeloid leukaemia

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

5.1.4. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - EMEA/H/C/005737

Scope: Active immunisation for prevention of coronavirus disease-2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in adults ≥18 years old

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

5.1.5. Istradefylline - EMEA/H/C/005308

Scope: Adjunctive treatment to levodopa-based regimens in patients with Parkinson's disease

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

5.1.6. Lenadogene nolparvovec - EMEA/H/C/005047, Orphan

Applicant: GenSight Biologics S.A., ATMP[3]

Scope: Treatment of vision loss due to Leber hereditary optic neuropathy (LHON)

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

5.1.7. Lonafarnib - EMEA/H/C/005271, Orphan

Applicant: EigerBio Europe Limited

[3] Advanced therapy medicinal product

Scope (accelerated assessment): Treatment of Hutchinson-Gilford progeria syndrome and progeroid laminopathies

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

5.1.8. Odevixibat - EMEA/H/C/004691, Orphan

Applicant: Albireo

Scope (accelerated assessment): Treatment of progressive familial intrahepatic cholestasis (PFIC)

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

5.1.9. Roxadustat - EMEA/H/C/004871

Scope: Treatment of anaemia

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

5.1.10. Selumetinib - EMEA/H/C/005244, Orphan

Applicant: AstraZeneca AB

Scope: Treatment of neurofibromatosis type 1 (NF1)

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

5.1.11. Tirbanibulin mesilate - EMEA/H/C/005183

Scope: Topical field treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis

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

5.1.12. Tralokinumab - EMEA/H/C/005255

Scope: Treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy

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. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/II/0169

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 16.1) to remove registry study GS-EU-276-4487 (as a category 3 study in the RMP): a prospective, longitudinal, observational registry of emtricitabine/tenofovir disoproxil fumarate for human immunodeficiency virus 1 (HIV-1) pre-exposure prophylaxis (PrEP) in the European Union

Action: For adoption of PRAC Assessment Report

5.2.2. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0025

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 7.1) in order to amend the study population for study C0168Z03 (PSOLAR): a multicentre open registry of patients with psoriasis who are candidates for systemic therapy including biologics. As a consequence, the MAH submitted an amendment to the protocol previously agreed in June 2018 for the registry study

Action: For adoption of PRAC Assessment Report

5.2.3. Melatonin - CIRCADIN (CAP) - EMEA/H/C/000695/II/0061

Applicant: RAD Neurim Pharmaceuticals EEC SARL

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 7.0) to remove the following risks from the list of potential risks: drug interaction with levothyroxine, panic attacks, potential interaction with warfarin, sperm motility decreased/spermatozoa morphology abnormal and withdrawal. Furthermore, the MAH took the opportunity to introduce minor corrections throughout the RMP

Action: For adoption of PRAC Assessment Report

5.2.4. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/II/0020

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 1.1) in order to amend the list of important identified risks, to update data concerning PASS studies and to change the submission due date of the final results of study PUMA-NER-6201 (MEA 001): an open-label study to characterize the incidence and severity of diarrhoea in patients with early stage human epidermal growth factor receptor 2 positive (HER2+) breast cancer treated with neratinib and intensive loperamide prophylaxis, with/without anti-inflammatory treatment (budesonide) and with/without a bile acid sequestrant (colestipol), from Q1 2021 to Q4 2021

Action: For adoption of PRAC Assessment Report

5.2.5. Rotavirus vaccine (live, oral) - ROTATEQ (CAP) - EMEA/H/C/000669/II/0085

Applicant: MSD Vaccins

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 7.2) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems'. As a consequence, the list of safety

concerns is updated and a reclassification of important risks is proposed. In addition, the updated RMP includes the removal of hypersensitivity and severe combined immunodeficiency (SCID) from the list of safety concerns as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002666/201911) adopted in June 2020

Action: For adoption of PRAC Assessment Report

5.2.6. Rotigotine - LEGANTO (CAP) - EMEA/H/C/002380/WS2000/0035; NEUPRO (CAP) - EMEA/H/C/000626/WS2000/0089

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 5.0) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.7. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/WS1805/0057; MODIGRAF (CAP) - EMEA/H/C/000954/WS1805/0035; NAP

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

Scope: Submission of an updated RMP (version 3) in order to add a non-interventional study related to the safety concerns of use during pregnancy and use during lactation. The MAH took the opportunity to combine the two important potential risks of 'exchangeability between the granule and capsule formulations of tacrolimus' for Modigraf (tacrolimus) and 'if administered accidentally either arterially or perivascularly, the reconstituted solution may cause irritation at the injection site' for Prograf (tacrolimus) concentrate for solution for infusion into the important identified risk of 'medication errors'. Finally, the RMP is updated in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.8. Trabectedin - YONDELIS (CAP) - EMEA/H/C/000773/II/0061

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 9.0) in order to reflect new available data from completed studies, removal of safety concerns and removal of a target follow-up questionnaire. The RMP is also brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.9. Zoledronic acid - ACLASTA (CAP) - EMEA/H/C/000595/II/0076

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 13.0) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' including consequential removal/reclassification of a number of important potential risks; to remove the education material on renal dysfunction and use in patients with severe renal impairment; to remove 'post-dose symptoms' from the list of important identified risks as per the conclusions of LEG 037 adopted in September 2019 and variation II/74/G adopted in March 2020; to update of the targeted questionnaire related to osteonecrosis of the jaw (ONJ) as per the conclusions of LEG 035 adopted in January 2017; to include the completed 5-year registry for study ZOL446H2422 (listed as a category 3 study in the RMP): a non-interventional post-authorisation safety study using health registries to compare safety of Aclasta (zoledronic acid) against oral bisphosphonates and untreated population controls as per the conclusions of variation II/69 adopted in January 2018. The additional risk minimisation measures in Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' are updated accordingly

Action: For adoption of PRAC Assessment Report

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

5.3.1. Abemaciclib - VERZENIOS (CAP) - EMEA/H/C/004302/II/0013

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include Verzenios (abemaciclib) in combination with endocrine therapy for adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1 and 5.3 of the SmPC are updated. 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

5.3.2. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0069

Applicant: Bayer AG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of sections 4.2 and 5.1 of the SmPC for the indication of the treatment of visual impairment due to diabetic macular oedema (DME) based on results from the post-authorisation efficacy study (PAES) study 17613 (VIOLET): an open-label, randomized, active-controlled, parallel-group, phase-3b study of the efficacy, safety, and tolerability of three different treatment regimens of 2 mg aflibercept administered by intravitreal injections to subjects with DME. The submission also includes data from study AQUA: an open-label phase-4 study to examine the change of vision-related quality of life in subjects with DME during treatment with intravitreal injections of 2 mg aflibercept according to EU label for the first year of treatment, which served as run-in study for VIOLET. The RMP (version 28.1) is updated accordingly

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

5.3.3. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0052

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include Tecentriq (atezolizumab) in combination with nab-paclitaxel and anthracycline-based chemotherapy for the neoadjuvant treatment of adult patients with locally advanced or early triple negative breast cancer (TNBC) based on the results of the pivotal study WO39392 (IMpassion031): a phase 3 randomized study to investigate the efficacy and safety of atezolizumab in combination with neoadjuvant anthracycline/nab-paclitaxel-based chemotherapy compared with placebo and chemotherapy in patients with primary invasive triple-negative breast cancer. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the Tecentriq (atezolizumab) 840 mg concentrate for solution for infusion SmPC and section 4.8 of the Tecentriq (atezolizumab) 1,200 mg concentrate for solution for infusion SmPC are updated. The package leaflet and the RMP (version 18.0) are updated in accordance

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

5.3.4. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0053

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of the final report from study GO29322 (listed as a category 3 study in the RMP): a phase 1b study investigating the safety and pharmacology of atezolizumab administered with ipilimumab, interferon-alpha, or other immune modulating therapies in patients with locally advanced or metastatic solid tumours. The RMP (version 19.0) is updated accordingly

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

5.3.5. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0028, Orphan

Applicant: Kite Pharma EU B.V., ATMP[4]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC to update the safety information based on updates from study KTE-C19-101: a phase 1/2 multicentre study evaluating the safety and efficacy of Yescarta (axicabtagene ciloleucel (KTE-C19)) in subjects with refractory aggressive non-Hodgkin lymphoma (ZUMA-1). The updates include data from: 1) phase 2 safety management ZUMA-1 cohort 4 intended to assess the impact of earlier interventions on the rate and severity of cytokine release syndrome (CRS) and neurologic events; 2) a 36-month analysis from ZUMA-1 cohorts 1 and 2. The RMP (version 3.1) is updated accordingly

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

[4] Advanced therapy medicinal product

and CHMP

5.3.6. Bortezomib - BORTEZOMIB ACCORD (CAP) - EMEA/H/C/003984/X/0023

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Amelia Cupelli

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (2.5 mg/mL, solution for injection). The RMP (version 11.0) is updated accordingly

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

5.3.7. Buprenorphine - BUVIDAL (CAP) - EMEA/H/C/004651/X/0008/G

Applicant: Camurus AB

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped applications consisting of: 1) line extension to add a new strength of 160 mg for prolonged-release solution for injection pharmaceutical form. The RMP (version 1.1) is updated accordingly. The MAH took the opportunity to align the product information with the latest quality review of documents (QRD) template (version 10.1) and to implement new text regarding the content of ethanol in accordance with the EMA document on 'information for the package leaflet regarding ethanol used as an excipient in medicinal products for human use' in the package leaflet; 2) quality/manufacturing aspect related variation

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

5.3.8. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/II/0021, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.2 of the SmPC in order to modify administration instructions to include the option of self/carer-administration based on results from two interventional clinical safety and efficacy studies, namely: 1) study KRN23-003: a phase 3 open-label trial to assess the efficacy and safety of burosumab (KRN23) in paediatric patients with X-linked hypophosphatemic rickets/osteomalacia (final study report); 2) study KRN23-004: a phase 3 long-term extension study of burosumab in adult patients with X-linked hypophosphataemic Rickets/osteomalacia and a post-marketing study of burosumab switched from the phase 3 long-term extension study (interim report). The package leaflet is updated accordingly and includes a new section with instructions for use. In addition, the MAH took the opportunity to implement editorial changes throughout the product information. The RMP (version 3.0) is also updated in accordance

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

5.3.9. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/II/0017

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include in combination with nivolumab first line treatment of advanced renal cell carcinoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 5.0) are updated in accordance

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

5.3.10. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS1941/0043; FORXIGA (CAP) - EMEA/H/C/002322/WS1941/0062

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include treatment of chronic kidney disease. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Forxiga and Edistride (dapagliflozin) are updated based on the results from the renal outcomes study D169AC00001 (DAPA-CKD) (listed as a category 3 study in the RMP): a multicentre, event-driven, randomized, double-blind, parallel group, placebo-controlled study evaluating the effect of dapagliflozin versus placebo given once daily in addition to standard of care to evaluate the potential risk of lower limb amputation to prevent the progression of chronic kidney disease (CKD) or cardiovascular (CV)/renal death. Annex II-B on 'Conditions or restrictions regarding supply and use' and the package leaflet are updated accordingly. The RMP (version 22.1) is also updated in accordance

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

5.3.11. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0043, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include treatment of adult patients with systemic light chain (AL) amyloidosis. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 8.2) are updated in accordance

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

5.3.12. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0044, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication for Darzalex (daratumumab) subcutaneous formulation to include combination with pomalidomide and dexamethasone for the treatment of adult patients with relapsed and refractory multiple myeloma (RRMM), whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, section 4.8 of the SmPC for

the intravenous formulation is updated based on pooled safety analysis data. The package leaflet and the RMP (version 8.2) are updated in accordance

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

5.3.13. Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/X/0145

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension application to introduce a new pharmaceutical form (gastro-resistant tablets). The RMP (version 14.0) is updated in accordance

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

5.3.14. Delafloxacin - QUOFENIX (CAP) - EMEA/H/C/004860/II/0003

Applicant: A. Menarini Industrie Farmaceutiche Riunite s.r.l.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include treatment of community acquired pneumonia (CAP) for Quofenix (delafloxacin) 450 mg tablets and 300 mg powder for concentrate for solution for infusion. 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 2.0) are updated in accordance

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

5.3.15. Dengue tetravalent vaccine (live, attenuated) - DENGVAXIA (CAP) - EMEA/H/C/004171/II/0016/G

Applicant: Sanofi Pasteur

PRAC Rapporteur: Sonja Hrabcik

Scope: Grouped variations consisting of an update of section 4.5 of the SmPC to include co-administration data on Gardasil/Cervarix (human papillomavirus vaccine) and Adacel (tetanus toxoid/reduced diphtheria toxoid and acellular/pertussis vaccine (adsorbed)) based on the final results of studies (listed as category 3 studies in the RMP) dedicated to immunogenicity and safety of the concomitant administration, namely: 1) study CYD66: a phase 3b, randomized, multicentre, open-label study in 688 subjects aged from 9 to 60 years in the Philippines; 2) CYD67: a phase 3b, randomized, open-label, multicentre study in 528 subjects aged 9 to 13 years in Malaysia; 3) CD71: a phase 3b, randomized, open-label, multicentre study in 480 female subjects aged 9 to 14 years in Mexico. The package leaflet and the RMP (version 6.1) 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 RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.16. Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/II/0013/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of: 1) update of section 4.8 of the SmPC to add alopecia, oral sores and rash in line with revised clinical safety data; 2) update of sections 4.8 and 5.1 of the SmPC based on the study report from 5-year open-label study 20120178: a phase 2, multicentre, randomized, double-blind, placebo-controlled, parallel-group study of subjects with episodic migraine; 3) update of section 5.1 of the SmPC to include of the anatomical therapeutic chemical (ATC) classification system code for erenumab. The package leaflet and the RMP (version 3.0) are updated accordingly

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

5.3.17. Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/WS1953/0013; ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/WS1953/0012

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC of Steglatro (ertugliflozin) and Segluromet (ertugliflozin/metformin) in order to modify the indication, update posology recommendations and include efficacy and safety information based on the final results from study 8835-004/B1521021 (listed as a category 3 study in the RMP): a multicentre, multinational, randomised, double-blind, placebo-controlled study to evaluate the effect of ertugliflozin on cardiovascular risk in adult patients with type 2 diabetes (T2DM) and established atherosclerotic cardiovascular disease (VERTIS CV study). 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

5.3.18. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - EMEA/H/C/004313/II/0015

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC for Steglujan (ertugliflozin/sitagliptin) in order to update clinical information following the final results from study 8835-004/B1521021 (listed as a category 3 study in the RMP): a multicentre, multinational, randomised, double-blind, placebo-controlled study to evaluate the effect of ertugliflozin on cardiovascular risk in adult patients with type 2 diabetes (T2DM) and established atherosclerotic cardiovascular disease (VERTIS CV study). The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to include an editorial change in section 4.1 of the SmPC

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

5.3.19. Glecaprevir, pibrentasvir - MAVIRET (CAP) - EMEA/H/C/004430/X/0033/G

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form (50/20 mg coated granules in sachet); 2) extension of indication to include the treatment of children from 3 to 12 years of age for the approved Maviret

(glecaprevir/pibrentasvir) 100 mg/40 mg film-coated tablets. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The package leaflet, labelling and the RMP (version 5.0) are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.20. Glecaprevir, pibrentasvir - MAVIRET (CAP) - EMEA/H/C/004430/II/0039

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of section 5.1 of the SmPC based on results from study M13-576 (listed as a category 3 study in the RMP): a non-drug interventional follow-up study to assess resistance and durability of response to AbbVie direct-acting antiviral agent (DAA) therapy (glecaprevir (ABT-493) and/or pibrentasvir (ABT-530)) in subjects who participated in phase 2 or 3 clinical studies for the treatment of chronic hepatitis C virus (HCV) infection. The RMP (version 6.0) is updated accordingly

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

5.3.21. Insulin aspart - INSULIN ASPART SANOFI (CAP) - EMEA/H/C/005033/X/0003

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Annika Folin

Scope: Extension application to introduce a new route of administration (intravenous use) for the 10 mL vial presentations only. The RMP (version 1.1) is updated accordingly

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

5.3.22. Isatuximab - SARCLISA (CAP) - EMEA/H/C/004977/II/0003, Orphan

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to add combination with carfilzomib and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 1.0) are updated accordingly. The MAH took the opportunity to introduce minor changes in sections 4.9, 6.3 and 6.6 of the SmPC and to update details of the local representatives

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

5.3.23. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0003, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report for study VX18-445-007 (study 007) (listed as a category 3 study in the RMP) with the aim to evaluate the pharmacokinetics (PK) of Kaftrio (ivacaftor/tezacaftor/elexacaftor) in subjects with moderate hepatic impairment. The RMP (version 1.2) is updated accordingly

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

5.3.24. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/II/0041

Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: Update of sections 4.5 and 5.1 of the SmPC in order to update the drug-drug interaction with everolimus and to update the efficacy information based on the results from study E7080-M001-221: a single-arm, multicentre, phase 2 trial to evaluate the safety and efficacy of lenvatinib in combination with everolimus in subjects with unresectable advanced or metastatic non clear cell renal cell carcinoma (nccRCC) who have not received any chemotherapy for advanced disease (in fulfilment of MEA 008.1). The RMP (version 12.1) is updated accordingly

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

5.3.25. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/II/0042

Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: Submission of the final clinical study report (CSR) for study E7080-G000-218: a randomised, open-label (formerly double-blind), phase 2 trial to assess safety and efficacy of lenvatinib at two different starting doses (18 mg vs 14 mg once a day (QD)) in combination with everolimus (5 mg QD) in renal cell carcinoma following one prior Vascular endothelial growth factor (VEGF)-targeted treatment (in fulfilment of MEA 007.3). The RMP (version 12.2) is updated accordingly

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

5.3.26. Lorlatinib - LORVIQUA (CAP) - EMEA/H/C/004646/II/0013

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to include hypertension and hyperglycaemia as new adverse drug reactions (ADRs) with frequency common and very common respectively together with recommended dose modifications and warnings, based on data from study B7461006: a phase 3, randomized, open-label study of lorlatinib monotherapy versus crizotinib monotherapy in the first-line treatment of patients with advanced anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC). In addition, the pooled safety dataset has been updated to include data from study B7461001: a phase 1/2 open-label, multiple-dose, dose-escalation, safety, pharmacokinetic, pharmacodynamic and anti-tumour efficacy exploration study; and study B7461006. As a consequence, the frequencies of ADRs have been updated in section 4.8 of

the SmPC and existing warnings on hyperlipidaemia and lipase and amylase increase have been amended. The package leaflet and the RMP (version 2.0) is updated accordingly

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

5.3.27. Nitisinone - NITISINONE MDK (CAP) - EMEA/H/C/004281/X/0007

Applicant: MendeliKABS Europe Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Extension application to add a new strength of 20 mg (hard capsule). The RMP (version 2.0) is updated accordingly

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

5.3.28. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0092

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include Opdivo (nivolumab) in combination with cabozantinib for the first line treatment of advanced renal cell carcinoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 19.0) are updated in accordance

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

5.3.29. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/II/0021

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.4 in order to include the term 'anaphylaxis' among the possible symptoms of infusion-related reactions (IRRs), following an analysis of cases retrieved by anaphylactic reaction MedDRA[5] narrow standardised MedDRA queries (SMQ). The MAH took the opportunity to update Annex II-C on 'Other conditions and requirements of the marketing authorisation' and Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' 'in line with the latest quality review of documents (QRD) template (version 10.1). The RMP (version 6.0) is updated accordingly

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

5.3.30. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0042

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to add myelodysplastic syndrome (MDS)/acute myeloid leukaemia (AML) to the list of adverse drug reactions with the frequency uncommon, to modify the existing warning on MDS/AML and to update

[5] Medical Dictionary for Regulatory Activities

efficacy information based on final results from study SOLO-2 (listed as a post-authorisation efficacy study (PAES) in Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product'): a phase 3 randomised, double blind, placebo controlled, multicentre study of olaparib maintenance monotherapy in platinum sensitive relapsed BRCA[6] mutated ovarian cancer patients who are in complete or partial response following platinum based chemotherapy. The package leaflet, Annex II and the RMP (version 21.1) are updated accordingly

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

5.3.31. Pegaspargase - ONCASPAR (CAP) - EMEA/H/C/003789/II/0036/G

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of: 1) submission of the results for study 12-266 A(12): an open label single arm phase 2 trial evaluating the efficacy and toxicity of treatment regimens including Oncaspar (pegaspargase) in adults aged 18-60 with newly diagnosed Philadelphia chromosome-negative acute lymphoblastic leukaemia ; 2) submission of the results for study CAALL-F01: a prospective multicentre cohort study evaluating Oncaspar (pegaspargase) used in the first-line treatment of children and adolescents with acute lymphoblastic leukaemia (ALL) along with multi-agent chemotherapy. As a consequence, Annex II is updated to remove both studies (i.e. post-authorisation safety studies (PAES)). Additionally, the product information is updated to remove the need for additional monitoring and to implement editorial changes. The RMP (version 4.1) is updated accordingly

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

5.3.32. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0097

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include in combination with chemotherapy, first-line treatment of locally advanced unresectable or metastatic carcinoma of the oesophagus or human epidermal growth factor receptor 2 (HER2) negative gastroesophageal junction adenocarcinoma in adults based on the results from the pivotal KEYNOTE-590 (KN590) trial: a phase 3, randomized, double-blind, placebo-controlled, multisite study to evaluate the efficacy and safety of pembrolizumab in combination with chemotherapy (cisplatin and 5-fluorouracil (5-FU)) versus chemotherapy (cisplatin with 5-FU) as first line treatment in participants with locally advanced unresectable metastatic adenocarcinoma or squamous cell carcinoma of the oesophagus or advanced/metastatic Siewert type 1 adenocarcinoma of the gastroesophageal junction. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 30.1) are updated in accordance

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

[6] BReast CAncer gene

5.3.33. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/X/0012

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension application to add a new strength of 150 mg for solution for injection in a pre-filled syringe and pre-filled pen. The RMP (version 2.0) is updated accordingly

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

5.3.34. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/X/0067

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension application to introduce a new strength of 75 mg solution for injection. The RMP (version 8.0) is updated accordingly

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

5.3.35. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/X/0045/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped application consisting of: 1) extension application to introduce a new strength (200 mg /50 mg /50 mg film-coated tablets). The new presentation is indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients aged 12 years and older or weighing at least 30 kg. In addition, the MAH took the opportunity to implement minor editorial updates in module 3.2.P; 2) Extension of indication to include paediatric use in patients aged 12 years and older or weighing at least 30 kg to the existing presentation. Sections 4.2, 4.8, 5.1 and 5.2 of the SmPC and the package leaflet are updated to support the extended indication. The RMP (version 3.2) is updated in accordance

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

5.3.36. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/X/0031/G

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of: 1) extension application to add a new strength of 7 mg film-coated tablet for use in paediatric patients from 10 years of age and older with relapsing remitting multiple sclerosis (MS); 2) extension of indication to include treatment of paediatric patients aged 10 years and older with relapsing remitting MS for Aubagio (teriflunomide) 14 mg tablet. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet, labelling and the RMP (version 6.0) are updated in accordance. The MAH also applied for an extension of the market protection of one additional year in line with the guidance on elements required to support significant clinical benefit in comparison with existing therapies of a new therapeutic indication

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

5.3.37. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/X/0030/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped application consisting of: 1) extension application to add a new strength (22 mg prolonged-release tablet); 2) update of sections 4.1, 4.2, 4.4 , 4.8, 5.1 and 5.2 of Xeljanz 11 mg prolonged-release tablets SmPC in order to include the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent, as an alternative to the immediate release film-coated tablets. Section 4.2 of the SmPC of Xeljanz film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of UC. The package leaflet and the RMP (version 15.1) are updated accordingly

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

5.3.38. Trastuzumab - HERCEPTIN (CAP) - EMEA/H/C/000278/II/0168

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to modify the administration instructions by removing the observation time currently stipulated after administration and to amend the existing warning respectively based on final results from study MO28048 (SafeHER) (listed as a category 3 study in the RMP): a phase 3 prospective, two cohort non-randomized, multicentre, multinational, open label study to assess the safety of assisted- and self-administered subcutaneous Herceptin as adjuvant therapy in patients with operable human epidermal growth factor receptor 2 (HER2)-positive early breast cancer. The package leaflet and the RMP (version 22) are updated accordingly

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

5.3.39. Trastuzumab - ZERCEPAC (CAP) - EMEA/H/C/005209/II/0003

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Addition of a new fill weight for Zercepac (trastuzumab) powder for concentrate for solution for infusion, 60mg/vial. The strength (concentration after reconstitution) is identical to the previously authorised finished product 150mg/vial presentation. The RMP (version 1.1) is updated accordingly

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

5.3.40. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/X/0006/G

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Grouped variations consisting of: 1) extension application to introduce a new

strength (30 mg prolonged-release tablet); 2) extension of indication to add treatment of moderate to severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated in accordance. In addition, the MAH took the opportunity to include a minor update in Annex II

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. Aclidinium bromide - BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP) - PSUSA/00009005/202007

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alectinib - ALECENSA (CAP) - PSUSA/00010581/202007

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alirocumab - PRALUENT (CAP) - PSUSA/00010423/202007

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Ambrisentan - VOLIBRIS (CAP) - PSUSA/00000129/202006

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/202007

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Avanafil - SPEDRA (CAP) - PSUSA/00010066/202006

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Beclometasone, formoterol, glycopyrronium bromide - RIARIFY (CAP); TRIMBOW (CAP); TRYDONIS (CAP) - PSUSA/00010617/202007

Applicant(s): Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Birch bark extract[7] - EPISALVAN (CAP) - PSUSA/00010446/202007

Applicant: Amryt GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Botulinum toxin type B - NEUROBLOC (CAP) - PSUSA/00000428/202006

Applicant: Sloan Pharma S.a.r.l

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Brexpiprazole - RXULTI (CAP) - PSUSA/00010698/202007

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Michal Radik

[7] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Brinzolamide, brimonidine tartrate - SIMBRINZA (CAP) - PSUSA/00010273/202006

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Brodalumab - KYNTHEUM (CAP) - PSUSA/00010616/202007

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Budesonide[8] - JORVEZA (CAP) - PSUSA/00010664/202007

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/202007

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Cenegermin - OXERVATE (CAP) - PSUSA/00010624/202007

Applicant: Dompe farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[8] Centrally authorised product(s) only

6.1.16. Cladribine[9] - MAVENCLAD (CAP) - PSUSA/00010634/202007

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Darolutamide - NUBEQA (CAP) - PSUSA/00010843/202007

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Evolocumab - REPATHA (CAP) - PSUSA/00010405/202007

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Glecaprevir, pibrentasvir - MAVIRET (CAP) - PSUSA/00010620/202007

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Glucagon[10] - BAQSIMI (CAP) - PSUSA/00010826/202007

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Guselkumab - TREMFYA (CAP) - PSUSA/00010652/202007

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

[9] Indicated for the treatment of multiple sclerosis only
[10] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Idursulfase - ELAPRASE (CAP) - PSUSA/00001722/202007

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Imipenem, cilastatin, relebactam - RECARBRIO (CAP) - PSUSA/00010830/202007

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Inotersen - TEGSEDI (CAP) - PSUSA/00010697/202007

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. L-lysine hydrochloride, l-arginine hydrochloride - LYSAKARE (CAP) - PSUSA/00010786/202007

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Lonoctocog alfa - AFSTYLA (CAP) - PSUSA/00010559/202007

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Macimorelin - MACIMORELIN AETERNA ZENTARIS (CAP) - PSUSA/00010746/202007

Applicant: Aeterna Zentaris GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Metreleptin - MYALEPTA (CAP) - PSUSA/00010700/202007

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Nateglinide - STARLIX (CAP) - PSUSA/00002128/202006

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Neratinib - NERLYNX (CAP) - PSUSA/00010712/202007

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Nivolumab - OPDIVO (CAP) - PSUSA/00010379/202007

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Osilodrostat - ISTURISA (CAP) - PSUSA/00010820/202007

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Palivizumab - SYNAGIS (CAP) - PSUSA/00002267/202006

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Peginterferon alfa-2a - PEGASYS (CAP) - PSUSA/00009254/202007

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Peginterferon beta-1a - PLEGRIDY (CAP) - PSUSA/00010275/202007

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Perampanel - FYCOMPA (CAP) - PSUSA/00009255/202007

Applicant: Eisai GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Romosozumab - EVENITY (CAP) - PSUSA/00010824/202007

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Saxagliptin, dapagliflozin - QTERN (CAP) - PSUSA/00010520/202007

Applicant: AstraZeneca AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - PSUSA/00010619/202007

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - PSUSA/00010630/202007

Applicant: CO.DON AG, ATMP[11]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.41. Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/202007

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Tigecycline - TYGACIL (CAP) - PSUSA/00002954/202006

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Voretigene neparvovec - LUXTURNA (CAP) - PSUSA/00010742/202007

Applicant: Novartis Europharm Limited, ATMP[12]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

[11] Advanced therapy medicinal product
[12] Advanced therapy medicinal product

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

6.2.1. Aripiprazole - ABILIFY (CAP); ABILIFY MAINTENA (CAP); ARIPIPRAZOLE SANDOZ (CAP); NAP - PSUSA/00000234/202007

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

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Caffeine[13] - PEYONA (CAP); NAP - PSUSA/00000482/202007

Applicant(s): Chiesi Farmaceutici S.p.A. (Peyona), various

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Albendazole (NAP) - PSUSA/00000073/202007

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Alfacalcidol (NAP) - PSUSA/00000080/202006

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Almotriptan (NAP) - PSUSA/00000101/202006

Applicant(s): various

[13] Indicated in primary apnoea of premature newborns

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Ascorbic acid, paracetamol, phenylephrine hydrochloride (NAP) - PSUSA/00000255/202006

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Benzylpenicillin (NAP) - PSUSA/00000383/202006

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Bethanechol (NAP) - PSUSA/00000402/202006

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Betula verrucosa[14] [15] [16] (NAP) - PSUSA/00010815/202007

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Carrageenin, titanium dioxide, zinc oxide (NAP); carrageenin, lidocaine, titanium dioxide, zinc oxide (NAP); titanium dioxide, zinc oxide, tetracaine hydrochloride (NAP) - PSUSA/00001869/202006

Applicant(s): various

PRAC Lead: Melinda Palfi

[14] Allergen for therapy
[15] Sublingual tablet(s) only
[16] Decentralised authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Clonazepam (NAP) - PSUSA/00000812/202006

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Diphtheria, tetanus, pertussis (acellular, component), poliomyelitis (inactivated) vaccine (adsorbed) (NAP); diphtheria, tetanus, pertussis (acellular, component), poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content) (NAP) - PSUSA/00001126/202007

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Epirubicin (NAP) - PSUSA/00001234/202006

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Ethinylestradiol, etonogestrel (NAP) - PSUSA/00001307/202007

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Hepatitis A (inactivated), typhoid polysaccharide vaccine (adsorbed) (NAP) - PSUSA/00001594/202006

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Ibuprofen, pseudoephedrine (NAP) - PSUSA/00001711/202007

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Iohexol (NAP) - PSUSA/00001768/202006

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Iopromide (NAP) - PSUSA/00001773/202006

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Lidocaine, tetracaine (NAP) - PSUSA/00001868/202006

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide (NAP) - PSUSA/00010390/202007

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Magnesium sulfate (NAP) - PSUSA/00009225/202006

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Nitrous oxide (NAP); nitrous oxide, oxygen (NAP) - PSUSA/00010572/202006

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Octenidine (NAP) - PSUSA/00010748/202007

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Octreotide (NAP) - PSUSA/00002201/202006

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Oxytocin (NAP) - PSUSA/00002263/202006

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Primidone (NAP) - PSUSA/00002525/202006

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/LEG 011.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to LEG 011 [detailed review of cases with potential increase of immunosuppression-related serious infections, opportunistic infections and varicella-zoster infections when baricitinib is used in combination with other rheumatoid arthritis (RA) drugs as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010578/201908) adopted in March 2020] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Evolocumab - REPATHA (CAP) - EMEA/H/C/003766/II/0047

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 4.8 of the SmPC in order to add myalgia to the list of adverse drug reactions (ADRs) with a frequency common following the review of nonclinical, clinical, post-marketing safety, and external spontaneous reporting databases as requested in the as requested in the conclusions of the latest periodic safety update report single assessment (PSUSA) procedure (PSUSA/00010405/201907) adopted in February 2020. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to add a traceability statement in line with a statement previously added to the SmPC and to propose minor updates to instructions for use of evolocumab SureClick pre-filled pen for enhanced usability

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[17]

6.6.1. Coronavirus (COVID-19) mRNA[18] vaccine (nucleoside-modified) BNT162b1 - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Second expedited monthly summary safety report for Comirnaty (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

[17] 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

[18] Messenger ribonucleic acid

Action: For adoption of PRAC Assessment Report

6.6.2. Coronavirus (COVID-19) mRNA[19] vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/ MEA 011

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: First expedited monthly summary safety report for COVID-19 Vaccine Moderna (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.3. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/MEA 017.6

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Eighth expedited summary safety report for Veklury (remdesivir) 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)[20]

7.1.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/PSP/S/0087.1

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to PSP/S/0087 [protocol for a non-interventional PASS to investigate the risk of mortality in patients prescribed Lemtrada (alemtuzumab) relative to comparable patients using other disease modifying therapies: a cohort study] as per the request for supplementary information (RSI) adopted in October 2020

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

7.1.2. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/PSP/S/0088.1

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to PSP/S/0087 [protocol for a non-interventional PASS to

[19] Messenger ribonucleic acid
[20] In accordance with Article 107n of Directive 2001/83/EC

investigate drug utilisation and safety monitoring patterns for Lemtrada (alemtuzumab)] as per the request for supplementary information (RSI) adopted in October 2020

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

7.1.3. Blinatumomab – BLINCYTO (CAP) - EMEA/H/C/PSA/S/0065

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Substantial amendment to a protocol previously agreed in November 2017 (PSA/S/0024) for study 20150136 (EUPAS17848): an observational study of blinatumomab safety and effectiveness, utilisation and treatment practices in order to characterise the safety of blinatumomab in routine clinical practice, its effectiveness, medication errors and utilisation

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

7.1.4. Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/PSA/S/0064

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: Substantial amendment to a protocol previously agreed in October 2020 (PSA/S/0050.1) for study ALX-HPP-501: an observational, longitudinal, prospective, long-term registry of patients with hypophosphatasia to collect information on the epidemiology of the disease, including clinical outcomes and quality of life, and to evaluate safety and effectiveness data in patients treated with Strensiq (asfotase alfa)

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

7.1.5. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/PSP/S/0089

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study BLU-285-1406: an observational study evaluating safety and efficacy of avapritinib in the first line treatment of patients with platelet derived growth factor alpha D842V mutated gastrointestinal stromal tumour (GIST)

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

7.1.6. Valproate (NAP) - EMEA/H/N/PSA/J/0063

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Substantial amendment to a joint protocol previously agreed in September 2020 (PSA/J/0059) for a joint survey among healthcare professionals (HCP) to assess the knowledge of HCP and behaviour with regard to the pregnancy prevention programme (PPP), the receipt/use of direct healthcare professional communication (DHPC) and

educational materials as well as for a survey among patients to assess the knowledge of patients with regards to PPP and receipt/use of educational materials, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[21]

7.2.1. Cannabidiol - EPIDYOLEX (CAP) - EMEA/H/C/004675/MEA 007.1

Applicant: GW Pharma (International) B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 007 [protocol for study GWEP19022 (listed as a category 3 study in the RMP): a long-term safety study to assess the potential for chronic liver injury in patients treated with Epidyolex (cannabidiol oral solution)] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.2. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - COVID-19 VACCINE ASTRAZENECA (CAP) - EMEA/H/C/005675/MEA 005

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Protocol for study D8111R00003(EU) (D8110R00001 (US)): a phase 4 enhanced active surveillance study of people vaccinated with AZD1222 (COVID-19 Vaccine AstraZeneca (COVID-19 vaccine)) (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CHMP

7.2.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - COVID-19 VACCINE ASTRAZENECA (CAP) - EMEA/H/C/005675/MEA 006

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Protocol for study AZD1222 pregnancy registry: a pregnancy registry of women exposed to AZD1222 (COVID-19 Vaccine AstraZeneca (COVID-19 vaccine)) immediately before or during pregnancy (C-VIPER) (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CHMP

7.2.4. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/MEA 006.2

Applicant: Eli Lilly Nederland B.V.

[21] 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

PRAC Rapporteur: Ilaria Baldelli

Scope: MAH's response to MEA 006.1 [protocol for study H9X-MC-B013 (listed as a category 3 study in the RMP): a non-interventional retrospective study to estimate the incidence rates of events of interest among type 2 diabetes mellitus (T2DM) patients treated with dulaglutide compared to other glucagon-like peptide 1 (GLP-1) receptor agonists in order to better characterise the safety profile of dulaglutide in terms of acute pancreatitis, pancreatic and thyroid malignancies] as per the request for supplementary information (RSI) adopted in May 2020

Action: For adoption of advice to CHMP

7.2.5. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 007.1

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 007 [protocol for study TEG4005: a pregnancy surveillance programme of infants and women exposed to Tegsedi (inotersen) during pregnancy] as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

7.2.6. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/MEA 009.4

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Martin Huber

Scope: Substantial amendment to a protocol previously agreed in September 2019 for a PASS: linaclotide safety study assessing the complications of diarrhoea and associated risk factors in selected European populations with irritable bowel syndrome with constipation (IBS-C) for Constella (linaclotilde) 290µg capsule

Action: For adoption of advice to CHMP

7.2.7. Micafungin - MYCAMINE (CAP) - EMEA/H/C/000734/MEA 015.13

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 015.12 [protocol for study 9463-PV-0002 (listed as a category 3 study in the RMP): a non-interventional PASS/survey on the effectiveness of the updated prescriber checklist for Mycamine (micafungin)] as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

7.2.8. Osilodrostat - ISTURISA (CAP) - EMEA/H/C/004821/MEA 003.1

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 003 [protocol for registry LCI699-RECAG-CL 0565: a multi-country, observational study to collect clinical information on patients with endogenous Cushing's syndrome treated with osilodrostat and to document the long-term safety [final study results expected in December 2027]] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.9. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 003.2

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 003.1 [protocol for study 165-501: a multicentre, prospective global observational study to evaluate the long term safety of subcutaneous injections of pegvaliase in patients with phenylketonuria [final clinical study report (CSR) expected in Q2 2030]] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.10. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 002.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002.2 [protocol for study P16-751 on pregnancy exposures and outcomes in psoriasis patients treated with risankizumab: a cohort study utilising large healthcare databases with mother-baby linkage in the United States [final study report expected in Q3 2026]] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.11. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/MEA 016.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 016.1 [amendment to a protocol previously agreed by CHMP for study B3461001: a sub-analysis of 'transthyretin amyloidosis outcomes survey (THAOS)': a global, multicentre, longitudinal, observational survey of patients with documented transthyretin (TTR) gene mutations or wild-type ATTR amyloidosis, in order to evaluate the effects of tafamidis in non-V30M patients] as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

7.2.12. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 013.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 013.1 [protocol for study A3921344 (listed as a category 3 study in the RMP): an active surveillance, post-authorisation study to characterise the safety of tofacitinib in patients with moderately to severely active ulcerative colitis (UC) in the real-world setting using data from the Swedish Quality Register for Inflammatory Bowel Disease (SWIBREG) registry as requested in the conclusions of procedure X/0005/G finalised in May 2018 and in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1485) finalised in November 2019] as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

7.2.13. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 014.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 014.1 [protocol for study A3921321: a drug utilisation study (DUS) on the utilisation and prescribing patterns of Xeljanz (tofacitinib) in two European countries using administrative claims databases and national registries for assessment, as requested in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1485) finalised in November 2019] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.2.14. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 047.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 047 [protocol for study SWIBREG-UST UC: an observational PASS to describe the safety of ustekinumab and other ulcerative colitis treatments in a cohort of patients with ulcerative colitis using the Swedish Inflammatory Bowel Disease Register (SWIBREG) as requested in the conclusions of variation II/071 finalised in July 2019 [final clinical study report (CSR) expected in May 2027]] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.15. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 048.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 048 [protocol for study SNDS-UST UC: an observational PASS to describe the safety of ustekinumab and other ulcerative colitis treatments in a cohort of patients with ulcerative colitis using the French administrative healthcare database (SNDS[22]) as requested in the conclusions of variation II/071 finalised in July 2019 [final

[22] Système National des Données de Santé

clinical study report (CSR) expected in May 2027]] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[23]

None

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

7.4.1. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/II/0030

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Submission of the final report from study BO40643 (listed as a category 3 study in the RMP): a non-interventional PASS aimed at evaluating the effectiveness of the risk minimisation measures (RMMs) for the important identified risks of interstitial lung disease (ILD)/pneumonitis, hepatotoxicity, bradycardia, photosensitivity, severe myalgia, and creatine phosphokinase (CPK) elevations for Alecensa (alectinib)

Action: For adoption of PRAC Assessment Report

7.4.2. Anakinra - KINERET (CAP) - EMEA/H/C/000363/II/0078

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final report from study Sobi-ANAKIN-201 (listed as a category 3 study in the RMP): a non-interventional PASS to evaluate the safety of Kineret (anakinra) in the treatment of cryopyrin associated periodic syndromes (CAPS) in routine clinical care with regard to serious infections, malignancies, injection site reactions, allergic reactions and medication errors, including reuse of syringe. The RMP (version 5.4) is updated accordingly. In addition, the RMP is updated to include information about a completed paediatric study (Sobi.ANAKIN-301) assessed as per Article 46 of Regulation No 1901/2006 (P46/031): a randomised, double-blind, placebo-controlled, multicentre, phase 3 study which evaluated the efficacy, safety, pharmacokinetics and immunogenicity of anakinra as compared to placebo in newly diagnosed Still's disease patients (including systemic juvenile idiopathic arthritis [SJIA] and adult-onset Still's disease [AOSD])

Action: For adoption of PRAC Assessment Report

7.4.3. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/II/0042, Orphan

Applicant: Janssen-Cilag International NV

[23] In accordance with Article 107p-q of Directive 2001/83/EC
[24] 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

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report for study TMC207TBC4002 (listed as a category 3 study in the RMP): a non-interventional multi-country multidrug-resistant tuberculosis patient registry in South Africa and South Korea to monitor bedaquiline safety, utilisation and emergence of resistance (in fulfilment of MEA 010.6). The RMP (version 8.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0051

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of the final study report for study B009 (listed as a category 3 study in the RMP): a multi-database collaborative research programme of observational studies to monitor the drug utilisation and safety of dulaglutide in the EU (in fulfilment of MEA 002). The RMP (version 6.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. Florbetaben (^{18}F) - NEURACEQ (CAP) - EMEA/H/C/002553/II/0033

Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study FBB-01_03_13 (PASS-2) (listed as a category 3 study in the RMP): a non-interventional, cross-sectional, retrospective, multicentre, multi-country registry to observe usage pattern, safety and tolerability of the diagnostic agent NeuraCeq (florbetaben (^{18}F)) in European clinical practice. The RMP (version 5.9) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Insulin detemir - LEVEMIR (CAP) - EMEA/H/C/000528/II/0101

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy, based on final results from non-interventional study NN304-4016 (listed as a category 3 study in the RMP): a diabetes pregnancy registry study conducted to assess the long-term safety of insulin use in pregnant women. The RMP (version 21.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. Meningococcal group B vaccine (recombinant, component, adsorbed) - BEXSERO (CAP) - EMEA/H/C/002333/II/0098

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study V72_36OB (205512) (listed as a category 3 study in the RMP): an observational PASS after Bexsero (meningococcal group B vaccine) vaccination within the UK National Immunisation Programme (NIP) by further characterising the important potential risks of seizures, vasculitis/Kawasaki syndrome (KD), anaphylaxis, acute disseminated encephalomyelitis (ADEM) and Guillain-Barré syndrome (GBS) in routine UK care. The RMP (version 9.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. Nitisinone - ORFADIN (CAP) - EMEA/H/C/000555/II/0074

Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final report from study Sobi.NTBC-005 (listed as a category 3 study in the RMP): a non-interventional PASS to evaluate the long-term safety of Orfadin (nitisinone) treatment in hereditary tyrosinaemia type 1 (HT-1) patients in standard clinical care. The RMP (version 5.3) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.9. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0082

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final safety registry report of study CNTO1275PSO4005 (listed as a category 3 study in the RMP): a Nordic database initiative for exposure to ustekinumab - a review and analysis of adverse events from the Swedish and Danish national registry systems. The RMP (version 18.2) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.10. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/II/0049, Orphan

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of final physician data study results for study EUPASS 14255: an evaluation of the effectiveness of risk minimisation measures - a survey among healthcare professionals (HCPs) and patient/caregivers to assess their knowledge and attitudes on prescribing and home administration conditions of velaglucerase alfa (Vpriv) in 6 European countries

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. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/MEA 001.4

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study F-FR-60000-001 (CASSIOPE): a prospective non-interventional study of the utilisation of cabozantinib tablets in adults with advanced renal cell carcinoma (RCC) following prior vascular endothelial growth factor (VEGF)-targeted therapy in real life settings in terms of dose modifications due to adverse events (AEs) when used as a second line therapy or third and later line therapy

Action: For adoption of advice to CHMP

7.5.2. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/MEA 002.3

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Fourth annual progress report for study 242-12-402 (listed as a category 3 study in the RMP): a multicentre EU-wide observational non-interventional post-authorisation study to assess the safety and drug usage of delamanid (OPC-67683) in routine medical practice in multidrug-resistant tuberculosis patients (Delamanid registry)

Action: For adoption of advice to CHMP

7.5.3. Filgrastim - NIVESTIM (CAP) - EMEA/H/C/001142/MEA 015.5

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Fourth annual report for study ZOB-NIV-1513 (C1121008): a multinational, multicentre, prospective, non-interventional PASS in healthy donors (HDs) exposed to Nivestim (biosimilar filgrastim) for haematopoietic stem cell (HSC) mobilisation (NEST) [final clinical study report (CSR) expected in March 2023]

Action: For adoption of advice to CHMP

7.5.4. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/MEA 002.6

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Interim results for study INSLIC08571(listed as a category 3 study in the RMP): a cross-sectional multinational, multichannel survey conducted among healthcare professionals and patients to measure the effectiveness of Suliqua (insulin glargine/lixisenatide) educational materials set up to evaluate the knowledge and understanding of the key safety messages in the healthcare professional guide and the

patient guide

Action: For adoption of advice to CHMP

7.5.5. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/ANX 003.5

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Fourth annual report for study VX14 809 108: an observational study to evaluate the utilisation patterns and long-term effects of lumacaftor/ivacaftor therapy in patients with cystic fibrosis (CF) [final report expected in December 2021] together with MAH's response to ANX 003.4 [third annual report for study VX14 809 108] as per the request for supplementary information (RSI) adopted in February 2020

Action: For adoption of advice to CHMP

7.5.6. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/ANX 001.3

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Third annual interim study report for study P15-11: a multicentre, observational PASS to document the drug utilisation of Wakix (pitolisant) and to collect information on the safety of Wakix (pitolisant) when used in routine medical practice [final results expected in 2023]

Action: For adoption of advice to CHMP

7.5.7. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/ANX 003.4

Applicant: Novartis Europharm Limited, ATMP[25]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: First five-yearly interim report for a study based on disease registry CCTL019B2401 (listed as a category 1 study in Annex II and the RMP): a non-interventional PASS in acute lymphoblastic leukaemia (ALL) and diffuse large B-cell lymphoma (DLBCL) patients in order to further characterise the safety, including long-term safety, of Kymriah (tisagenlecleucel) [final study report expected in December 2038]

Action: For adoption of advice to CAT and CHMP

7.5.8. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/MEA 005

Applicant: Novartis Europharm Limited, ATMP[26]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: First five-yearly interim report for study CCTL019A2205B (listed as a category 3

[25] Advanced therapy medicinal product
[26] Advanced therapy medicinal product

study in the RMP): a long-term follow-up of patients exposed to lentiviral-based CD[27]19 directed chimeric antigen receptor T (CAR-T)-cell therapy in order to describe selected, delayed adverse events (AEs) suspected to be related to previous CD19 CAR-T-cell therapy as outlined in current Health Authority guidelines [final study report expected in December 2037] (from opinion/marketing authorisation)

Action: For adoption of advice to CAT and CHMP

7.5.9. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.21

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 022.20 [ninth annual report for study C0168Z03 (PSOLAR: PSOriasis Longitudinal Assessment and Registry): an international prospective cohort study/registry programme designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.5.10. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 024.15

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 024.14 [tenth annual interim report for study CNTO1275PSO4007 (Nordic pregnancy research initiative) (C0743T): exposure to ustekinumab during pregnancy in patients with psoriasis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.5.11. Voriconazole - VFEND (CAP) - EMEA/H/C/000387/MEA 091.4

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Third interim report for non-interventional study A1501103: an active safety surveillance programme to monitor selected events in patients with long-term voriconazole use

Action: For adoption of advice to CHMP

[27] Cluster of differentiation

7.6. Others

7.6.1. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/MEA 002

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Interim progress report for study 19764: an interventional post-marketing investigation (PMI) to assess safety and efficacy of Jivi (damoctocog alfa pegol (BAY 94-9027) treatment in participants with haemophilia A to fulfil EMA guidelines regarding the requirements for applications of marketing authorisation for recombinant or plasma derived factor VIII products [final study report expected by 2023]

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Cholic acid - ORPHACOL (CAP) - EMEA/H/C/001250/S/0038 (without RMP)

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/S/0051 (without RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/S/0064 (with RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

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. Betibeglogene autotemcel - ZYNTEGLO (CAP) - EMEA/H/C/003691/R/0018 (without RMP)

Applicant: bluebird bio (Netherlands) B.V, ATMP[28]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.2. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/R/0027 (without RMP)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Atazanavir - ATAZANAVIR MYLAN (CAP) - EMEA/H/C/004048/R/0016 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

[28] Advanced therapy medicinal product

8.3.2. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/R/0029 (without RMP)

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP[29]

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.3.3. Bortezomib - BORTEZOMIB HOSPIRA (CAP) - EMEA/H/C/004207/R/0020 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Bortezomib - BORTEZOMIB SUN (CAP) - EMEA/H/C/004076/R/0015 (without RMP)

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/R/0018 (with RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/R/0026 (with RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

[29] Advanced therapy medicinal product

8.3.7. Methotrexate - NORDIMET (CAP) - EMEA/H/C/003983/R/0018 (without RMP)

Applicant: Nordic Group B.V.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Pemetrexed - PEMETREXED FRESENIUS KABI (CAP) - EMEA/H/C/003895/R/0023 (with RMP)

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/R/0038 (with RMP)

Applicant: Teva B.V.

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. Onasemnogene abeparvovec – ZOLGENSMA (CAP) - EMEA/H/C/004750/II/0008

Applicant: Novartis Gene Therapies EU Limited, ATMP[30]

PRAC Rapporteur: Ulla Wändel Liminga

Scope: PRAC consultation on a variation to update sections 4.4 and 4.8 of the SmPC to add thrombotic microangiopathy. The package leaflet is updated accordingly

Action: For adoption of advice to CAT and CHMP

10.1.2. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/II/0031

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: PRAC consultation on a variation to update sections 4.2 and 4.4 of the SmPC on tumour lysis syndrome (TLS) prophylaxis and management following an update to the company core data sheet (CCDS) as result of a medical safety assessment conducted on TLS post-marketing reports

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.

[30] Advanced therapy medicinal product

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Iopamidol (NAP) - IE/H/xxxx/WS/137

Applicant(s): Bracco Imaging SPA (Niopam)

PRAC Lead: Ronan Grimes

Scope: PRAC consultation on a worksharing variation procedure evaluating several safety topics, namely: contrast induced encephalopathy, neonatal hypothyroidism, drug reaction with eosinophilia and systemic symptoms (DRESS) and persistence in the foetus/neonate secondary to transplacental passage, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure (PSUSA/00001771/201912) concluded in September 2020, on request of Ireland

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q4 2020

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

12.3.1. CHMP Scientific Advice Working Party (SAWP) PRAC working group – SAWP members - new appointments

Action: For adoption

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.4.2. Incident Review Network (IRN) – call for interest for a PRAC representative: renewal of composition of the EU regulatory network incident management plan for medicines for human use

Action: For discussion

12.4.3. PRAC strategic review and learning meeting (SRLM) under the Portuguese presidency of the European Union (EU) Council – Remote meeting, 19 March 2021 - agenda

PRAC Lead: Ana Sofia Diniz Martins, Marcia Sofia Sanches de Castro Lopes Silva

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

12.6.1. Coronavirus (COVID-19)-vaccines monitoring: ACCESS[31] consortium project - update

Action: For discussion

12.6.2. Coronavirus (COVID-19)-medicines monitoring: CONSIGN[32] consortium project – COVID-19 infection and medicines in pregnancy – update

PRAC Lead: Sabine Straus, Ulla Wändel Liminga

Action: For discussion

12.7. PRAC work plan

None

[31] vACcine Covid-19 monitoring readinESS
[32] Covid-19 infectiOn aNd medicineS In pregnancy

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q4 2020 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q4 2020

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC Lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC Lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.12.4. Adverse events of special interest (AESI) for coronavirus (COVID-19) vaccines – follow-up questionnaires

Action: For discussion

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Advanced therapy medicinal products (ATMPs) - EU data sources for long-term safety and efficacy follow-up

Action: For discussion

12.15.2. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. EMA pregnancy strategy - draft

Action: For discussion

12.20.2. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact: draft technical specifications for an impact study for methotrexate-containing products

PRAC Lead: Antoine Pariente

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/