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Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 07-10 June 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

07 June 2021, 10:30 – 19:30, via teleconference

08 June 2021, 08:30 – 19:30, via teleconference

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

10 June 2021, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

24 June 2021, 09:00 – 12:00, via teleconference

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

Note on access to documents

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



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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 07-10 June 2021. See June 2021 PRAC minutes (to be published post July 2021 PRAC meeting).

1.2. Agenda of the meeting on 07-10 June 2021

Action: For adoption

1.3. Minutes of the previous meeting on 03-06 May 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

None

3.2. Ongoing procedures

3.2.1. Betibeglogene autotemcel – ZYNTEGLO (CAP) – EMEA/H/A-20/1504

Applicant: Bluebird bio (Netherlands) B.V.; ATMP¹

PRAC Rapporteur: Brigitte Keller-Stanislawski; PRAC Co-rapporteur: Menno van der Elst

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

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

3.3. Procedures for finalisation

None

3.4. Re-examination procedures²

None

3.5. Others

None

4. Signals assessment and prioritisation³

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Adalimumab – AMGEVITA (CAP); AMSPARITY (CAP); HEFIYA (CAP); HULIO (CAP); HUMIRA (CAP); HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP); YUFLYMA (CAP)

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Humira), Amgen Europe B.V. (Amgevita), Celltrion Healthcare Hungary Kft. (Yuflyma), Fresenius Kabi Deutschland GmbH (Idacio), Mylan S.A.S (Hulio), Pfizer Europe MA EEIG (Amsparity), Samsung Bioepis NL B.V. (Imraldi), Sandoz GmbH (Hefiya, Hyrimoz)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of acquired haemophilia

Action: For adoption of PRAC recommendation

EPITT 19688 – New signal

¹ Advanced therapy medicinal product

² Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

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

Lead Member State(s): SE

4.1.2. Bupropion (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of acute generalised exanthematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 19704 – New signal

Lead Member State(s): NL

4.1.3. Lenvatinib – KISPLYX (CAP); LENVIMA (CAP)

Applicant(s): Eisai GmbH

PRAC Rapporteur: To be appointed

Scope: Signal of colitis

Action: For adoption of PRAC recommendation

EPITT 19691 – New signal

Lead Member State(s): SE

4.1.4. Lumacaftor, ivacaftor – ORKAMBI (CAP)

Applicant(s): Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

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

Action: For adoption of PRAC recommendation

EPITT 19702 – New signal

Lead Member State(s): IE

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

- 4.3.1. Cannabidiol – EPIDYOLEX (CAP); calcineurin inhibitors⁴: ciclosporin (NAP); tacrolimus - ADVAGRAF (CAP), ENVARSUS (CAP), MODIGRAF (CAP), TACFORIUS (CAP); NAP mammalian target of rapamycin (mTOR) inhibitors⁵: everolimus – AFINITOR (CAP),

⁴ For systemic use

⁵ For systemic use

VOTUBIA (CAP), NAP; sirolimus – RAPAMUNE (CAP); temsirolimus – TORISEL (CAP); NAP

Applicant(s): Astellas Pharma Europe B.V. (Advagraf, Modigraf), Chiesi Farmaceutici S.p.A. (Envarsus), GW Pharma (International) B.V. (Epidyolex), Novartis Europharm Limited (Afinitor, Votubia), Pfizer Europe MA EEIG (Rapamune, Torisel), Teva B.V. (Tacforius), various

PRAC Rapporteur: Ronan Grimes

Scope: Signal of drug interaction with cannabidiol leading to calcineurin inhibitors and mTOR inhibitors serum levels increased and toxicity

Action: For adoption of PRAC recommendation

EPITT 19614 – Follow-up to November 2020

4.3.2. Ceftriaxone (NAP)

Applicant(s): various

PRAC Rapporteur: Zane Neikena

Scope: Signal of hepatitis

Action: For adoption of PRAC recommendation

EPITT 19603 – Follow-up to February 2021

4.3.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/SDA/047

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of capillary leak syndrome

Action: For adoption of PRAC recommendation

EPITT 19672 – Follow-up to April 2021

4.3.4. Olanzapine – OLANZAPINE APOTEX (CAP); OLANZAPINE GLENMARK (CAP); OLANZAPINE GLENMARK EUROPE (CAP); OLANZAPINE MYLAN (CAP); OLANZAPINE TEVA (CAP); OLAZAX (CAP); OLAZAX DISPERSI (CAP); ZALASTA (CAP); ZYPADHERA (CAP) - EMEA/H/C/000890/SDA/030; ZYPREXA (CAP) - EMEA/H/C/000115/SDA/051; ZYPREXA VELOTAB (CAP) - EMEA/H/C/000287/SDA/044; NAP

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

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of cardiomyopathy

Action: For adoption of PRAC recommendation

EPITT 19663 – Follow-up to February 2021

4.3.5. [Tofacitinib - XELJANZ \(CAP\) - EMEA/H/C/004214/SDA/016](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of major adverse cardiovascular events (MACE) and malignancies excluding non-melanoma skin cancer (NMSC) from a clinical trial⁶

Action: For adoption of PRAC recommendation

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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. [Abrocitinib - EMEA/H/C/005452](#)

Scope: Treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy

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

5.1.2. [Artesunate - EMEA/H/C/005550, Orphan](#)

Applicant: Amivas Ireland Ltd

Scope: Treatment of malaria

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

5.1.3. [Dengue tetravalent vaccine \(live, attenuated\) - EMEA/H/W/005362](#)

Scope (accelerated assessment): Prevention of dengue disease

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

⁶ Study A3921133: a phase 3b/4 randomised safety endpoint study of 2 doses of tofacitinib in comparison to a tumour necrosis fibrosis (TNF) inhibitor in subjects with rheumatoid arthritis

5.1.4. [Dengue tetravalent vaccine \(live, attenuated\) - EMEA/H/C/005155](#)

Scope (accelerated assessment): Prevention of dengue disease

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

5.1.5. [Enfortumab vedotin - EMEA/H/C/005392](#)

Scope (accelerated assessment): Treatment of locally advanced (LA) or metastatic urothelial cancer (mUC)

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

5.1.6. [Fingolimod - EMEA/H/C/005661](#)

Scope: Treatment of multiple sclerosis

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

5.1.7. [Glucarpidase - EMEA/H/C/005467, Orphan](#)

Applicant: Protherics Medicines Development Europe B.V.

Scope: Treatment of patients at risk of methotrexate toxicity

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

5.1.8. [Lonapegsomatropin - EMEA/H/C/005367, Orphan](#)

Applicant: Ascendis Pharma Endocrinology Division A/S

Scope: Treatment of growth hormone deficiency

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

5.1.9. [Pegcetacoplan - EMEA/H/C/005553, Orphan](#)

Applicant: Apellis Ireland Limited

Scope: Treatment of paroxysmal nocturnal haemoglobinuria (PNH)

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

5.1.10. [Regdanvimab - EMEA/H/C/005854](#)

Applicant: Celltrion Healthcare Hungary Kft.

Scope: Treatment of coronavirus disease-2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

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

5.1.11. Ripretinib - EMEA/H/C/005614, Orphan

Applicant: Deciphera Pharmaceuticals (Netherlands) B.V.

Scope: Treatment of patients with advanced gastrointestinal stromal tumour (GIST)

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

5.1.12. Sacituzumab govitecan - EMEA/H/C/005182

Scope (accelerated assessment): Treatment of unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC)

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

5.1.13. Sodium thiosulfate - EMEA/H/C/005130, PUMA⁷

Scope: Prevention of ototoxicity induced by cisplatin (CIS) chemotherapy in patients of 1 month to < 18 years of age with localized, non-metastatic, solid tumours

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. Cholic acid - ORPHACOL (CAP) - EMEA/H/C/001250/II/0040, Orphan

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Submission of an updated RMP (version 4.0) in order to reflect the current status of the additional risk minimisation measures. Furthermore, the RMP is brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template) and the agreed protocol (PSA/S/0051) for a patient surveillance database to monitor accumulating data on efficacy and safety in the treatment of inborn errors in primary bile acid synthesis due to 3 β -hydroxy- Δ 5-C27-steroid oxidoreductase deficiency or Δ 4-3-oxosteroid-5 β -reductase deficiency with Orphacol (cholic acid) in infants, children, adolescents and adults as agreed as agreed in May 2020

Action: For adoption of PRAC Assessment Report

5.2.2. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/II/0015

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of an updated RMP (version 1.5) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to include long-term safety data from the completed PREMIERE registry: a prospective observational long-term safety registry of multiple sclerosis patients who have

⁷ Paediatric-use marketing authorisation(s)

participated in cladribine clinical studies; and to remove it from the pharmacovigilance plan. Furthermore, the status of the post-approval safety study MS 700568-0002: a long term, prospective, observational cohort study evaluating the safety profile in patients with highly active relapsing multiple sclerosis (RMS) newly started on oral cladribine (CLARION); and study MS 700568-0004: pregnancy outcomes in women exposed to oral cladribine: a multi-country cohort database study (CLEAR) are updated. Finally, the RMP is updated in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010634/201907) adopted in January 2020

Action: For adoption of PRAC Assessment Report

5.2.3. [Desloratadine - AERIUS \(CAP\) - EMEA/H/C/000313/WS2057/0098; AZOMYR \(CAP\) - EMEA/H/C/000310/WS2057/0102; NEOCLARITYN \(CAP\) - EMEA/H/C/000314/WS2057/0096](#)

Applicant: Organon N.V.

PRAC Rapporteur: Laurence de Fays

Scope: Submission of an updated RMP (version 2.1) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template), which includes updates to the list of safety concerns. It also reflects the completion of study EUPAS15038 (listed as a category 3 study in the RMP): a Nordic register-based study which studied the association between the use of desloratadine and risk of seizures, supraventricular tachycardia, and atrial fibrillation or flutter as per the conclusions of procedure WS1655 finalised in January 2020

Action: For adoption of PRAC Assessment Report

5.2.4. [Fulvestrant - FASLODEX \(CAP\) - EMEA/H/C/000540/II/0073](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Update of the RMP (version 13) in line with revision 2 of GVP module V on 'Risk management systems' resulting in the removal of additional risk minimisation measures for important identified risks and reclassification of safety concerns as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001489/202004) adopted in January 2021

Action: For adoption of PRAC Assessment Report

5.2.5. [Ibritumomab tiuxetan - ZEVALIN \(CAP\) - EMEA/H/C/000547/II/0053](#)

Applicant: Ceft Biopharma s.r.o.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 5.0) in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.6. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2043/0087; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2043/0102

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 19.3 for Opdivo, version 31 for Yervoy) to change the final due date for the post-authorisation efficacy study (PAES) study CA2098Y8: a phase 3b, randomized, double-blind study of nivolumab combined with ipilimumab versus nivolumab monotherapy for patients with previously untreated advanced renal cell carcinoma and intermediate- or poor-risk factors, from '30 September 2021' to '30 June 2022'. In addition, the MAH took the opportunity to include a minor editorial revision in the French translation of the product information

Action: For adoption of PRAC Assessment Report

5.2.7. Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/WS1919/0109; PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/WS1919/0038

Applicant: Upjohn EESV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 13.0) to include results from recently completed PASS studies, namely: 1) study A0081359: a population-based cohort study of pregabalin to characterize pregnancy outcomes; 2) study A0081106: a 12-month open-label study to evaluate the safety and tolerability of pregabalin as adjunctive therapy in paediatric subjects 1 month to 16 years of age with partial onset seizures and paediatric and adult subjects 5 to 65 years of age with primary generalized tonic-clonic seizures; 3) study A0081042: a double-blind, placebo-controlled, parallel-group, multicentre study of the efficacy and safety of pregabalin as adjunctive therapy in children 1 month through <4 years of age with partial onset seizures; 4) study A0081105: a randomized, double-blind, placebo-controlled, parallel group, multicentre trial of pregabalin as adjunctive therapy in paediatric and adult subjects with primary generalized tonic-clonic seizures. In addition, information on study A0081096: a prospective randomized 12-week controlled study of visual field change in subjects with partial seizures receiving pregabalin or placebo has been updated as well as study A0081365: a phase 4, randomised, double-blind, double-dummy, placebo- and active-controlled, single-dose, six-way crossover study to evaluate the potential for abuse with pregabalin (added as a new FDA⁸-imposed PASS). The clinical study report (CSR) for study A0081359 is included in the submission

Action: For adoption of PRAC Assessment Report

5.2.8. Ritonavir - NORVIR (CAP) - EMEA/H/C/000127/II/0161

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 7.1) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). In addition, the MAH

⁸ United States Food and Drug Administration

reviewed the information contained in the RMP and removed the important identified risk of toxicity of Norvir (ritonavir) oral solution in preterm neonates, removed missing information regarding use of ritonavir in elderly patients. Finally, the MAH proposed to provide an analysis of the antiretroviral pregnancy registry (APR) data with the submission of PSUR

Action: For adoption of PRAC Assessment Report

5.2.9. [Sildenafil - REVATIO \(CAP\) - EMEA/H/C/000638/II/0091](#)

Applicant: Upjohn EESV

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 7.0) in line with revision 2 of GVP module V on 'Risk management systems'. Consequently, the educational programme for the risk of hypotension is proposed to be terminated

Action: For adoption of PRAC Assessment Report

5.2.10. [Simoctocog alfa - NUWIQ \(CAP\) - EMEA/H/C/002813/WS2064/0043; VIHUMA \(CAP\) - EMEA/H/C/004459/WS2064/0024](#)

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 11) to remove the following completed studies: 1) study GENA-05: immunogenicity, efficacy and safety of treatment with simoctocog alfa in previously untreated patients with severe haemophilia A; 2) study GENA-15: extension study for patients who completed GENA-05 (NuProtect)- to investigate immunogenicity, efficacy and safety of treatment with simoctocog alfa. As a consequence, 'safety in previously untreated patients', 'children < 2 years' and 'immune tolerance induction' are removed as missing information in the list of safety concerns. Finally, the RMP is brought in line with revision 2 of GVP module V on 'Risk management systems'

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. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/X/0004/G, Orphan

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Grouped applications consisting of: 1) line extension to add two new strengths of film-coated tablets (25 mg and 50 mg); 2) introduction of a new therapeutic indication to include treatment of adult patients with advanced systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) and mast cell leukaemia (MCL), after at least one systemic therapy for Ayvakyt (avapritinib) based on the results of study BLU-285-2101: a phase 1 study of avapritinib in patients with AdvSM and relapsed or refractory myeloid malignancies and study BLU-285-2202: An open-label, single arm, phase 2 study to evaluate efficacy and safety of avapritinib in patients with AdvSM. The new indication is applicable to the new and existing presentations (25 mg, 50 mg, 100 mg and 200 mg film-coated tablets). As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1, 5.2, 5.3, 6.1 and 8 of the SmPC are updated. The labelling, 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

5.3.3. Brivaracetam – BRIVIACT (CAP) – EMEA/H/C/003898/II/0032/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of: 1) extension of indication to include patients from 1 month to 4 years of age for treatment with Brivact (brivaracetam). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The RMP (version 8.0) is updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2). The MAH took the opportunity to implement minor editorial updates; 2) extension of the shelf life after the first opening of Brivact (brivaracetam) oral solution (supported by real time data); 3) addition of a 1 mL oral syringe and its adaptor for the paediatric population. The package leaflet and labelling are updated in accordance

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

5.3.4. Cabozantinib - COMETRIQ (CAP) - EMEA/H/C/002640/II/0044, Orphan

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Update of Annex II-E on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation' and section 5.1 of the SmPC to remove the specific obligation (SOB 001) and the reference to the conditional approval based on the final results from study XL184-401 (EXAMINER): a randomised, double-blind study to evaluate the efficacy and safety of cabozantinib (XL184) at 60 mg/day compared to a 140 mg/day in progressive, metastatic medullary thyroid cancer patients. The package leaflet and the RMP (version 5.4) are updated accordingly. As a consequence, the MAH proposed to revert from a conditional marketing authorisation to a full marketing

authorisation. Additionally, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.2 Rev 1) and to add information relating to sodium content in the product information in line with the guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. Finally, the MAH updated some details of local representatives

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

5.3.5. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/II/0020

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to change posology recommendations by adding an advice on preventive measures to avoid liver injury and to add a new warning on liver function and liver injury based on a review of post-approval data in MAH's safety database, non-clinical, clinical trial data and scientific literature. The package leaflet and the RMP (version 1.6) are updated accordingly

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

5.3.6. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0002

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.8, 5.1, 6.3 and 6.6 of the SmPC in order to update the safety profile and to add the adverse drug reactions: abdominal pain and urticaria with frequency uncommon and pain in extremity and influenza-like illness with frequency common based on the primary analysis from the pooled pivotal studies (listed as a specific obligation in the Annex II) namely: 1) study COV001: a phase 1/2 study to determine efficacy, safety and immunogenicity of the candidate coronavirus disease (COVID-19) vaccine ChAdOx1 nCoV-19 in UK healthy adult volunteers; 2) study COV002: a single-blind, randomised, controlled, phase 2/3 trial assessing the safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults conducted in the UK; 3) study COV003: a single-blinded, multicentre, randomised, controlled phase 3 trial assessing the safety, efficacy, and immunogenicity of AZD1222 in participants in Brazil; 4) study COV005: a blinded, multicentre, randomised, controlled phase 1/2 trial assessing the safety, efficacy, and immunogenicity of AZD1222 in participants in South Africa. The MAH took the opportunity to introduce some editorial changes throughout the product information. The package leaflet, labelling and the RMP (version 2.1) are updated accordingly

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

5.3.7. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS2069/0048/G; FORXIGA (CAP) - EMEA/H/C/002322/WS2069/0067/G

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of the submission of the final study reports of the DETERMINE studies (listed as category 3 studies in the RMP): 1) study D169EC00001: an international, multicentre, parallel-group, randomised, double-blind, placebo-controlled, phase 3 study evaluating the effect of dapagliflozin on exercise capacity in patients with heart failure with preserved ejection fraction (HFpEF); 2) study D169EC00002: an international, multicentre, parallel-group, randomised, double-blind, placebo-controlled, phase 3 study evaluating the effect of dapagliflozin on exercise in patients with heart failure with reduced ejection fraction (HFrEF). The RMP (version 25) is updated accordingly

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

5.3.8. 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

5.3.9. 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, randomised, multicentre, open-label study in 688 subjects aged from 9 to 60 years in the Philippines; 2) study CYD67: a phase 3b, randomised, open-label, multicentre study in 528 subjects aged 9 to 13 years in Malaysia; 3) study CD71: a phase 3b, randomised, 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

5.3.10. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/II/0029

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include treatment of chronic hepatitis C (CHC) in paediatric patients 12 years of age and older who weigh at least 30 kg. 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 4.1) are updated in accordance. 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

5.3.11. Evolocumab - REPATHA (CAP) - EMEA/H/C/003766/II/0049/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped variations consisting of: 1) extension of indication to include a new paediatric indication in paediatric patients aged 10 years and over with heterozygous familial hypercholesterolaemia as an adjunct to diet, alone or in combination with other lipid-lowering therapy, to reduce low-density lipoprotein cholesterol (LDL-C) based on results of study 20120123 (HAUSER-RCT): a randomized, multicentre, placebo-controlled, double blind, parallel group, 24-week trial in 158 paediatric patients aged 10 to > 18 years with heterozygous familial hypercholesterolaemia. As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7.0) are updated in accordance; 2) extension of indications to modify the existing indication for treatment of adults and paediatric patients aged 10 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies based on interim results from study 20120124 (HAUSER-OLE): an open label, single arm, multicentre, 80-week trial to evaluate the safety, tolerability and efficacy of Repatha (evolocumab) for LDL-C reduction in paediatric patients from aged ≥ 10 to < 18 years of age with homozygous familial hypercholesterolaemia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly

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

5.3.12. Exenatide - BYETTA (CAP) - EMEA/H/C/000698/II/0075

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.2 and 5.1 of the SmPC based on the results of study H80-MC-GWBQ (assessed by CHMP as part of PAM P46 048): a 28-week, randomised, double-blind, placebo-controlled study to evaluate the safety and efficacy of exenatide twice daily in 120 patients aged 10 to 17 years; and study 2993-124: a randomised, single-blind, placebo-controlled, dose-rising study to evaluate the pharmacokinetic (PK), pharmacodynamic (PD) and tolerability of exenatide in adolescent patients. The RMP (version 35.1) is updated accordingly

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

5.3.13. Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/II/0061

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results from

study FAST (Febuxostat versus Allopurinol Streamlined Trial) (listed as a category 3 study in the RMP): an interventional study investigating the cardiovascular safety of febuxostat in comparison with allopurinol in patients with chronic symptomatic hyperuricaemia. The package leaflet and the RMP (version 8.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to update the warning relevant to the content of sodium according to the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.14. [Filgrastim - ACCOFIL \(CAP\) - EMEA/H/C/003956/II/0046/G](#)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of: 1) introduction of a new presentation Accofil 12 MU/0.2 mL solution for injection or infusion in pre-filled syringe; 2) introduction of a new presentation, Accofil 70 MU/0.73 mL solution for injection or infusion in pre-filled syringe. The product information and the RMP (version 5) are updated accordingly

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

5.3.15. [Guselkumab - TREMFYA \(CAP\) - EMEA/H/C/004271/II/0028](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC to reflect 5 years data from the final study reports of pivotal psoriasis studies (listed as category 3 studies in the RMP), namely: 1) study PSO3001: a phase 3, multicentre, randomized, double-blind, placebo and active comparator-controlled study evaluating the efficacy and safety of guselkumab in the treatment of subjects with moderate to severe plaque-type psoriasis; 2) study PSO3002: a phase 3, multicentre, randomized, double-blind, placebo and active comparator-controlled study evaluating the efficacy and safety of guselkumab for the treatment of subjects with moderate to severe plaque-type psoriasis with randomized withdrawal and retreatment. In the long-term extension part of these studies subjects received open-label guselkumab every 8 weeks (q8w) starting at week 52 in PSO3001 and at week 76 in PSO3002, with the last dose at week 252 and the last safety follow-up visit at week 264. The RMP (version 8.1) is 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. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/WS2048/0101; tezacaftor, ivacaftor - SYMKEVI \(CAP\) - EMEA/H/C/004682/WS2048/0030](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.2, 4.5, 4.8 and 5.1 of the SmPC to reflect the final clinical

study report (CSR) part A of study VX17-661-116: a phase 3, open-label, rollover study to evaluate the safety and efficacy of long-term treatment with tezacaftor in combination with ivacaftor in subjects with cystic fibrosis aged 6 years and older, homozygous or heterozygous for the F508del-cystic fibrosis transmembrane conductance regulator (CFTR) mutation. The package leaflet and the RMP (version 3.1 for Symkevi) are updated accordingly

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

5.3.17. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/WS2085/0099; ivacaftor, tezacaftor, elexacaftor - KAFTRIO \(CAP\) - EMEA/H/C/005269/WS2085/0014](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.4 and 4.8 of the SmPC following cases of liver failure reported in the post marketing setting. The package leaflet and the RMP (version 3.1 for Kaftrio) are updated accordingly

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

5.3.18. [Lacosamide - LACOSAMIDE UCB \(CAP\) - EMEA/H/C/005243/WS2049/0009/G; VIMPAT \(CAP\) - EMEA/H/C/000863/WS2049/0091/G](#)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped applications consisting of: 1) extension of indication to include patients from 1 month to 4 years of age for treatment of partial-onset seizures with or without secondary generalisation as monotherapy and adjunctive therapy. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The RMP (version 16.0) is updated accordingly; 2) change of a measuring or administration device; 3) change in the shelf-life or storage conditions of the finished product. The package leaflet and labelling are updated in accordance

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

5.3.19. [Lenvatinib - KISPLYX \(CAP\) - EMEA/H/C/004224/II/0045](#)

Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include lenvatinib in combination with pembrolizumab first line treatment of adults with advanced renal cell carcinoma (RCC). 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 13.0) are updated in accordance. 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

5.3.20. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/II/0042

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include lenvatinib in combination with pembrolizumab for the treatment of adult patients with advanced endometrial carcinoma (EC) who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 14.0) are updated in accordance. In addition, the MAH took the opportunity to make minor editorial changes to the SmPC and update the list of local representatives in the package leaflet in line with the latest quality review of documents (QRD) template (version 10.2)

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

5.3.21. 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

5.3.22. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/II/0036/G

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) extension of indication to include eosinophilic granulomatosis with polyangiitis (EGPA). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7) are updated in accordance. In addition, the MAH took the opportunity to update the local representative for Italy in the package leaflet; 2) addition of a new pack size of 9x100mg/mL multipack for pre-filled pens 100 mg/mL solution for injection and another pack size of 9x100mg/mL multipack for pre-filled syringes 100 mg/mL solution for injection. As a consequence, sections 6.5 and 8 of the SmPC and the package leaflet are updated accordingly. Annex III-A on 'labelling' is also updated to include information relating to the new pack sizes

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

5.3.23. Midostaurin - RYDAPT (CAP) - EMEA/H/C/004095/II/0018/G, Orphan

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Grouped variations consisting of: 1) update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with P-glycoprotein (P-gp), breast cancer resistance protein (BCRP) and cytochrome P450 2D6 (CYP2D6) substrates (digoxin, rosuvastatin, and dextromethorphan) based on final results from study CPKC412A2121 (listed as a category 3 study in the RMP): a phase 1, open-label, drug-drug interaction study. The package leaflet is updated accordingly (MEA 005.3); 2) update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with CYP2B6, CYP2C8, CYP3A4 substrates based on the final results from study CPKC412A2122 (listed as a category 3 study in the RMP): a phase 1, open-label, drug-drug interaction study. The package leaflet is updated accordingly (MEA 007.2); 3) update of sections 4.5 and 4.6 of the SmPC in order to add drug-drug interaction information with oral contraceptives and information on pregnancy and contraception based on final results from study CPKC412A2123 (listed as a category 3 study in the RMP): a phase 1, open-label, drug-drug interaction study. The package leaflet is updated accordingly (MEA 008.2); 4) update of section 5.2 of the SmPC in order to update pharmacokinetic information on organic anion transporting polypeptide 1B1 (OATP1B1) transporters based on final results from physiological based pharmacokinetic (PBPK) modelling study DMPK R2000528 (listed as category 3 study in the RMP) (MEA 009); 5) update of sections 4.2, 4.4 and 5.2 of the SmPC in order to amend posology instructions, an existing warning and pharmacokinetic information for patients with severe hepatic impairment based on final results from study CPKC412A2116 (listed as category 3 study in the RMP): an open label, multiple dose study to evaluate the pharmacokinetic (PK) of midostaurin in subjects with mild, moderate and severe hepatic impairment compared to matched healthy subjects (MEA010). The RMP (version 6.0) is updated accordingly. In addition, MAH took the opportunity to introduce minor changes to edit the wording related to the ethanol excipient in the package leaflet in line with the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668)

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

5.3.24. Migalastat - GALAFOLD (CAP) - EMEA/H/C/004059/II/0029, Orphan

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include long-term treatment of adolescents 12 to < 16 years with a confirmed diagnosis of Fabry disease (α -galactosidase A deficiency) and who have an amenable mutation. As a consequence, sections 4.1, 4.2, 4.8 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.25. [Netupitant, palonosetron - AKYNZEO \(CAP\) - EMEA/H/C/003728/X/0031](#)

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion). The RMP (version 2.8) is updated accordingly

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

5.3.26. [Nivolumab - OPDIVO \(CAP\) - EMEA/H/C/003985/II/0095](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include adjuvant treatment of adult patients with resected oesophageal, or gastro-oesophageal junction cancer who have residual pathologic disease following prior neoadjuvant chemoradiotherapy based on study CA209-577: a randomized, multicentre, double blind, phase 3 study of adjuvant nivolumab or placebo in subjects with resected oesophageal, or gastroesophageal junction cancer. 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 22.0) are updated in accordance

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

5.3.27. [Nivolumab - OPDIVO \(CAP\) - EMEA/H/C/003985/II/0100](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include adjuvant treatment of adults with muscle invasive urothelial carcinoma (MIUC) who are at high risk of recurrence after undergoing radical resection of MIUC. 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 23.0) are updated in accordance

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

5.3.28. [Obinutuzumab - GAZYVARO \(CAP\) - EMEA/H/C/002799/II/0044/G, Orphan](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include the administration of obinutuzumab as a short duration infusion (SDI) of approximately 90 minutes in patients with follicular lymphoma (FL) based on the end of induction safety and efficacy data from the ongoing phase 4 study MO40597 (GAZELLE): a multicentric, open-label, single arm study of obinutuzumab short duration infusion (SDI) in patients with previously untreated advanced FL. The package leaflet and the RMP (version 8.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet; 2) submission of an updated RMP (version 8.0) to change the due date for the submission of the final clinical safety report (CSR) for study

BO21223 (GALLIUM) (listed as a category 3 study in the RMP): a multicentre, phase 3, open-label, randomized study in previously untreated patients with advanced indolent non-Hodgkin's lymphoma evaluating the benefit of obinutuzumab plus chemotherapy compared with rituximab plus chemotherapy followed by obinutuzumab or rituximab maintenance therapy in responders, from Q4 2021 to Q1 2022; to remove important identified risks as per conclusions of the PSUR single assessment (PSUSA) (PSUSA/00010279/201910) concluded in May 2020; to correct the clinical cut-off dates and trial exposure data from previously conducted studies

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

5.3.29. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/II/0029, Orphan

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final results of study SHP634-101: an open-label, randomised, crossover study to assess the pharmacokinetic and pharmacodynamic profiles of once-daily and twice-daily dose regimens of recombinant human parathyroid hormone (rhPTH[1-84]) administered subcutaneously to subjects with hypoparathyroidism. Further clinical evaluation of an alternative dosing regimen is no longer warranted, as outlined in the current specific obligation (study SHP634-403). The conditional marketing authorisation can therefore be converted into a standard marketing authorisation (no longer subject to a specific obligation) valid for 5 years. The RMP (version 3.2) is updated accordingly

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

5.3.30. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0104

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include pembrolizumab in combination with lenvatinib first line treatment of adults with advanced renal cell carcinoma (RCC). As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 32.1) are updated in accordance

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

5.3.31. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0105

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include pembrolizumab in combination with lenvatinib for the treatment of advanced endometrial carcinoma in adults who have disease progression following prior systemic therapy in any setting and who are not candidates for curative surgery or radiation. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 33.1) are updated in accordance

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

5.3.32. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/II/0023/G, Orphan

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of an update of sections 4.2, 4.4, 4.5, 5.1 and 5.2 of the SmPC based on new clinical data from: 1) study P09-10 (HARMONY III): an open-label naturalistic pragmatic study to assess the long-term safety of pitolisant in the treatment of excessive daytime sleepiness (EDS) (with or without cataplexy) in narcolepsy; 2) study P16-02: a randomised, double-blind, active- and placebo-controlled, single-dummy, 4-way crossover study to determine the abuse potential of pitolisant compared to phentermine and placebo, in healthy, non-dependent recreational stimulant users. The proposed update also includes results of a post approval network meta-analysis which compares efficacy and safety of multiple treatments, multi-arm studies, and multi-criteria treatment decisions. The package leaflet and the RMP (version 6.0) are updated accordingly

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

5.3.33. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0050

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.2 and 5.1 of the SmPC to include the final results of study CINC424A2201 (EXPAND) (listed as a category 3 study in the RMP): a phase 1b open-label, dose-finding study intended to establish the maximum safe starting dose (MSSD) of ruxolitinib tablets administered orally to patients with myelofibrosis (MF) in previous unstudied population of patients who had baseline platelet counts $\geq 50 \times 10^9/L$ and $< 100 \times 10^9/L$. The package leaflet and the RMP (version 12.0) are updated accordingly. The RMP is also brought in line with revision 2 of GVP module V on 'Risk management systems' and in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010015/202002) adopted in October 2020

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

5.3.34. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0053

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include treatment of patients with graft versus host disease (GvHD) aged 12 years and older who have inadequate response to corticosteroids or other systemic therapies. 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 13.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives for the Netherlands in the package leaflet

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

5.3.35. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0076

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to introduce a new posology regimen for adult plaque psoriasis patients and psoriatic arthritis patients with concomitant moderate to severe plaque psoriasis based on the final results of study CAIN457A2324 (and exposure-response modelling): a randomised, double-blind, multicentre study assessing short (16 weeks) and long-term efficacy (up to 1 year), safety, and tolerability of sub-cutaneous secukinumab in subjects of body weight 90 kg or higher with moderate to severe chronic plaque-type psoriasis. The package leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.36. Ticagrelor - BRILIQUE (CAP) - EMEA/H/C/001241/II/0049

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include, in co-administration with acetylsalicylic acid (ASA), the prevention of stroke in adult patients with acute ischaemic stroke or transient ischaemic attack (TIA), based on the final results of study D5134C00003 (THALES): a phase 3, international, multicentre, randomised, double-blind, placebo-controlled study to investigate the efficacy and safety of ticagrelor and ASA compared with ASA in the prevention of stroke and death in patients with acute ischaemic stroke or transient ischaemic attack. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated in accordance

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/0024/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form (oral solution, 1 mg/mL); 2) addition of a new indication as treatment of active polyarticular juvenile idiopathic arthritis (pJIA) in patients of 2 years of age and older. The RMP (version 12.1) is updated in accordance. The MAH took the opportunity to align the product information 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

5.3.38. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0027

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC of Xeljanz (tofacitinib) 11 mg prolonged-release tablets in order to include the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease modifying antirheumatic drug therapy; as an alternative to the immediate release film-coated tablets. Section 4.2 of the SmPC for Xeljanz (tofacitinib) film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of PsA. The package leaflet and the RMP (version 13.1) are updated accordingly

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

5.3.39. [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 (trastuzumab) 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

5.3.40. [Trastuzumab emtansine - KADCYLA \(CAP\) - EMEA/H/C/002389/II/0055](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final clinical study report (CSR) of study MO28231 (KAMILLA): a two-cohort, open-label, multicentre study of trastuzumab emtansine (T-DM1) in human epidermal growth factor receptor 2 (HER2)-positive locally advanced or metastatic breast cancer patients who have received prior anti-HER2 and chemotherapy-based treatment in order to address the safety concerns of: ventricular dysfunction, safety in elderly patients and the use of a non-validated HER2 test. The RMP (version 13) is updated accordingly

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

5.3.41. [Upadacitinib - RINVOQ \(CAP\) - EMEA/H/C/004760/II/0009](#)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to amend the existing warning on vaccination based on the final results from vaccination sub-study within study M13-538 (listed as a category 3 study in the RMP): an open-label extension to assess the impact of upadacitinib treatment with a stable background of methotrexate on immunological responses following administration of a pneumococcal vaccine in rheumatoid arthritis

patients. The RMP (version 5.0) is updated accordingly

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. Acridinium bromide, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP); DUAKLIR GENUAIR (CAP) - PSUSA/00010307/202011

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Afatinib - GIOTRIF (CAP) - PSUSA/00010054/202009

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alpelisib - PIQRAY (CAP) - PSUSA/00010871/202011

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Andexanet alfa - ONDEXXYA (CAP) - PSUSA/00010764/202010

Applicant: Alexion Europe SAS

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Arsenic trioxide - TRISENOX (CAP) - PSUSA/00000235/202009

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. [Autologous CD34⁺ enriched cell fraction that contains CD34⁺ cells transduced with retroviral vector that encodes for the human adenosine deaminase \(ADA\) complementary deoxyribonucleic acid \(cDNA\) sequence - STRIMVELIS \(CAP\) - PSUSA/00010505/202011](#)

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP⁹

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.7. [Avatrombopag - DOPTelet \(CAP\) - PSUSA/00010779/202011](#)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. [Axicabtagene ciloleucel - YESCARTA \(CAP\) - PSUSA/00010703/202010](#)

Applicant: Kite Pharma EU B.V., ATMP¹⁰

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.9. [Benralizumab - FASENRA \(CAP\) - PSUSA/00010661/202011](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. [Bezlotoxumab - ZINPLAVA \(CAP\) - PSUSA/00010576/202010](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

⁹ Advanced therapy medicinal product

¹⁰ Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. [Buprenorphine¹¹ - SIXMO \(CAP\) - PSUSA/00010778/202011](#)

Applicant: L. Molteni & C. dei Fratelli Alitti Societa di Esercizio S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. [Cefiderocol - FETCROJA \(CAP\) - PSUSA/00010849/202011](#)

Applicant: Shionogi B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. [Ceftaroline fosamil - ZINFORO \(CAP\) - PSUSA/00010013/202010](#)

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. [Cetuximab - ERBITUX \(CAP\) - PSUSA/00000635/202009](#)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. [Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA \(CAP\) - PSUSA/00010449/202011](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹¹ Implant(s) only

6.1.16. Conestat alfa - RUCONEST (CAP) - PSUSA/00000873/202010

Applicant: Pharming Group N.V

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Crizanlizumab - ADAKVEO (CAP) - PSUSA/00010888/202011 (with RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dalbavancin - XYDALBA (CAP) - PSUSA/00010350/202011

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Daratumumab - DARZALEX (CAP) - PSUSA/00010498/202011

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Darbepoetin alfa - ARANESP (CAP) - PSUSA/00000932/202010

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Defibrotide - DEFITELIO (CAP) - PSUSA/00010086/202010

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Delamanid - DELTYBA (CAP) - PSUSA/00010213/202010

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Denosumab¹² - XGEVA (CAP) - PSUSA/00009119/202009

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Dinutuximab beta - QARZIBA (CAP) - PSUSA/00010597/202011

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Diphtheria, tetanus, pertussis antigens (pertussis toxoid, filamentous haemagglutinin, pertactin) (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated), haemophilus type b conjugate vaccines (adsorbed) - INFANRIX HEXA (CAP) - PSUSA/00001122/202010

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Dolutegravir, rilpivirine - JULUCA (CAP) - PSUSA/00010689/202011

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹² Indicated for skeletal related events associated with bone metastases and for giant cell tumour of bone

6.1.27. Durvalumab - IMFINZI (CAP) - PSUSA/00010723/202010

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Ebola Zaire vaccine (live, attenuated) - ERVEBO (CAP) - PSUSA/00010834/202011

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Edoxaban - LIXIANA (CAP); ROTEAS (CAP) - PSUSA/00010387/202010

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

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Emicizumab - HEMLIBRA (CAP) - PSUSA/00010668/202011

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Empagliflozin, linagliptin - GLYXAMBI (CAP) - PSUSA/00010539/202011

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Erenumab - AIMOVIG (CAP) - PSUSA/00010699/202011

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Etelcalcetide - PARSABIV (CAP) - PSUSA/00010533/202011

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Fexinidazole - FEXINIDAZOLE WINTHROP (Art 58¹³) - EMEA/H/W/002320/PSUV/0005

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.35. Fosamprenavir - TELZIR (CAP) - PSUSA/00001470/202010

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Fostamatinib - TAVLESSE (CAP) - PSUSA/00010819/202010

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Givosiran - GIVLAARI (CAP) - PSUSA/00010839/202011

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹³ Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

6.1.38. [Glasdegib - DAURISMO \(CAP\) - PSUSA/00010859/202011](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. [Glycopyrronium bromide, formoterol - BEVESPI AEROSPHERE \(CAP\) - PSUSA/00010739/202010](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. [Granisetron¹⁴ - SANCUSO \(CAP\) - PSUSA/00010101/202010](#)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. [Ibrutinib - IMBRUVICA \(CAP\) - PSUSA/00010301/202011](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. [Idarucizumab - PRAXBIND \(CAP\) - PSUSA/00010435/202010](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. [Indacaterol, glycopyrronium bromide - ULTIBRO BREEZHALER \(CAP\); ULUNAR BREEZHALER \(CAP\); XOTERNA BREEZHALER \(CAP\) - PSUSA/00010105/202009](#)

Applicant(s): Novartis Europharm Limited

¹⁴ Transdermal patch only

PRAC Rapporteur: Anette Kirstine Stark
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.44. Insulin degludec - TRESIBA (CAP); insulin degludec, insulin aspart - RYZODEG (CAP) - PSUSA/00010036/202009

Applicant(s): Novo Nordisk A/S
PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.45. Insulin glargine, lixisenatide - SULIQUA (CAP) - PSUSA/00010577/202011

Applicant: Sanofi-aventis groupe
PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.46. Irinotecan¹⁵ - ONIVYDE PEGYLATED LIPOSOMAL (CAP) - PSUSA/00010534/202010

Applicant: Les Laboratoires Servier
PRAC Rapporteur: David Olsen
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.47. Ixazomib - NINLARO (CAP) - PSUSA/00010535/202011

Applicant: Takeda Pharma A/S
PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.48. Ketoconazole¹⁶ - KETOCONAZOLE HRA (CAP) - PSUSA/00010316/202011

Applicant: HRA Pharma Rare Diseases
PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: Evaluation of a PSUSA procedure

¹⁵ Liposomal formulation(s) only

¹⁶ Centrally authorised product(s) only

Action: For adoption of recommendation to CHMP

6.1.49. Larotrectinib - VITRAKVI (CAP) - PSUSA/00010799/202011

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Letemovir - PREVYMIS (CAP) - PSUSA/00010660/202011

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Lurasidone - LATUDA (CAP) - PSUSA/00010114/202010

Applicant: Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Macitentan - OPSUMIT (CAP) - PSUSA/00010115/202010 (with RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Melatonin - CIRCADIN (CAP); SLENYTO (CAP) - PSUSA/00001963/202009

Applicant(s): RAD Neurim Pharmaceuticals EEC SARL

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - PSUSA/00010607/202010

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.55. [Mercaptamine¹⁷ - CYSTAGON \(CAP\); PROCYSBI \(CAP\) - PSUSA/00010573/202010](#)

Applicant(s): Chiesi Farmaceutici S.p.A. (Procysbi), Recordati Rare Diseases (Cystagon)
PRAC Rapporteur: Eva Segovia
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.56. [Midostaurin - RYDAPT \(CAP\) - PSUSA/00010638/202010](#)

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.57. [Necitumumab - PORTRAZZA¹⁸ - PSUSA/00010471/202011](#)

Applicant: Eli Lilly Nederland B.V.
PRAC Rapporteur: Rugile Pilviniene
Scope: Evaluation of a PSUSA procedure
Action: For discussion

6.1.58. [Nelarabine - ATRIANCE \(CAP\) - PSUSA/00002132/202010](#)

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Anette Kirstine Stark
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.59. [Nintedanib¹⁹ - OFEV \(CAP\) - PSUSA/00010319/202010](#)

Applicant: Boehringer Ingelheim International GmbH
PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

¹⁷ Treatment of nephropathic cystinosis only

¹⁸ European Commission (EC) decision on the marketing authorisation (MA) cessation of Portrazza dated 18 February 2021

¹⁹ Respiratory indication(s) only

6.1.60. [Obinutuzumab - GAZYVARO \(CAP\) - PSUSA/00010279/202010](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.61. [Onasemnogene abeparvovec - ZOLGENSMA \(CAP\) - PSUSA/00010848/202011](#)

Applicant: Novartis Gene Therapies EU Limited, ATMP²⁰

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.62. [Ozanimod - ZEPOSIA \(CAP\) - PSUSA/00010852/202011](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.63. [Padeliporfin - TOOKAD \(CAP\) - PSUSA/00010654/202011](#)

Applicant: Steba Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.64. [Pandemic influenza vaccine \(H5N1\) \(surface antigen, inactivated, adjuvanted\) - FOCLIVIA \(CAP\); prepandemic influenza vaccine \(H5N1\) \(surface antigen, inactivated, adjuvanted\) - AFLUNOV \(CAP\) - PSUSA/00010008/202010](#)

Applicant(s): Seqirus S.r.l

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.65. [Parathyroid hormone - NATPAR \(CAP\) - PSUSA/00010591/202010](#)

Applicant: Shire Pharmaceuticals Ireland Limited

²⁰ Advanced therapy medicinal product

PRAC Rapporteur: Rhea Fitzgerald
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.66. Pasireotide - SIGNIFOR (CAP) - PSUSA/00009253/202010

Applicant: Recordati Rare Diseases
PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.67. Patiromer - VELTASSA (CAP) - PSUSA/00010618/202010

Applicant: Vifor Fresenius Medical Care Renal Pharma France
PRAC Rapporteur: Kirsti Villikka
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.68. Pazopanib - VOTRIENT (CAP) - PSUSA/00002321/202010

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Anette Kirstine Stark
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.69. Pegvaliase - PALYNZIQ (CAP) - PSUSA/00010761/202011

Applicant: BioMarin International Limited
PRAC Rapporteur: Rhea Fitzgerald
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.70. Prasterone²¹ - INTRAROSA (CAP) - PSUSA/00010672/202011

Applicant: Endoceutics S.A.
PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

²¹ Pessary, vaginal use only

6.1.71. Regorafenib - STIVARGA (CAP) - PSUSA/00010133/202009

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.72. Remdesivir - VEKLURY (CAP) - PSUSA/00010840/202011

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.73. Rituximab - BLITZIMA (CAP); MABTHERA (CAP); RITEMVIA (CAP); RIXATHON (CAP); RIXIMYO (CAP); RUXIENCE (CAP); TRUXIMA (CAP) - PSUSA/00002652/202011

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

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.74. Rurioctocog alfa pegol - ADYNOVI (CAP) - PSUSA/00010663/202011

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.75. Sotagliflozin - ZYNQUISTA (CAP) - PSUSA/00010766/202010

Applicant: Guidehouse Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.76. Stiripentol - DIACOMIT (CAP) - PSUSA/00002789/202011

Applicant: BIOCINDEX

PRAC Rapporteur: Maia Uusküla
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.77. [Sulfur hexafluoride - SONOVUE \(CAP\) - PSUSA/00002822/202009](#)

Applicant: Bracco International B.V.
PRAC Rapporteur: Tiphaine Vaillant
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.78. [Susoctocog alfa - OBIZUR \(CAP\) - PSUSA/00010458/202011 \(with RMP\)](#)

Applicant: Baxalta Innovations GmbH
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.79. [Talazoparib - TALZENNA \(CAP\) - PSUSA/00010781/202010](#)

Applicant: Pfizer Europe MA EEIG
PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.80. [Talimogene laherparepvec - IMLYGIC \(CAP\) - PSUSA/00010459/202010](#)

Applicant: Amgen Europe B.V., ATMP²²
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CAT and CHMP

6.1.81. [Tenofovir alafenamide - VEMLIDY \(CAP\) - PSUSA/00010575/202011](#)

Applicant: Gilead Sciences Ireland UC
PRAC Rapporteur: Ilaria Baldelli
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

²² Advanced therapy medicinal product

6.1.82. Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/202011

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.83. Toremifene - FARESTON (CAP) - PSUSA/00002999/202009

Applicant: Orion Corporation

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.84. Turoctocog alfa - NOVOEIGHT (CAP) - PSUSA/00010138/202010

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.85. Vestronidase alfa - MEPSEVII (CAP) - PSUSA/00010709/202011

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.86. Volanesorsen - WAYLIVRA (CAP) - PSUSA/00010762/202011

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Bosentan - STAYVEER (CAP); TRACLEER (CAP); NAP - PSUSA/00000425/202011

Applicants: Janssen-Cilag International NV (Stayveer, Tracleer), various

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Insulin human - ACTRAPID (CAP), INSUMAN (CAP); insulin human, insulin isophane²³ - ACTRAPHANE (CAP), INSULATARD (CAP), MIXTARD (CAP), PROTAPHANE (CAP); NAP - PSUSA/00001753/202010

Applicants: Novo Nordisk A/S (Actraphane, Actrapid, Insulatard, Mixtard, Protaphane), Sanofi-Aventis Deutschland GmbH (Insuman), various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Micafungin - MYCAMINE (CAP); NAP - PSUSA/00002051/202010

Applicants: Astellas Pharma Europe B.V. (Mycamine), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Posaconazole - NOXAFIL (CAP); NAP - PSUSA/00002480/202010

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

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

²³ Subcutaneous and intravenous use only

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

6.3.1. ¹³C-methacetin (NAP) - PSUSA/00010846/202010

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Acitretin (NAP) - PSUSA/00000051/202010

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Adapalene, benzoyl peroxide (NAP) - PSUSA/00000059/202009

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Amlodipine, atorvastatin, perindopril (NAP) - PSUSA/00010431/202010

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Atorvastatin, perindopril (NAP) - PSUSA/00010679/202010

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Baclofen²⁴ (NAP) - PSUSA/00000294/202009

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Beractant (NAP) - PSUSA/00000384/202010

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Bisoprolol (NAP) - PSUSA/00000419/202009

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Bisoprolol, perindopril (NAP) - PSUSA/00010462/202010

Applicant(s): various

PRAC Lead: Michal Radik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Calcium carbonate, famotidine, magnesium hydroxide (NAP) - PSUSA/00001351/202009

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Clevidipine (NAP) - PSUSA/00010288/202011

Applicant(s): various

PRAC Lead: Jan Neuhauser

²⁴ Oral use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Desflurane (NAP) - PSUSA/00000958/202009

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Desogestrel, ethinylestradiol (NAP) - PSUSA/00000967/202009

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Epinephrine, lidocaine (NAP) - PSUSA/00001233/202009

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Etifoxine (NAP) - PSUSA/00001321/202010

Applicant(s): various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Human von Willebrand factor (NAP) - PSUSA/00001642/202009

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Hydroxyzine (NAP); hydroxyzine chloride, hydroxyzine pamoate²⁵ (NAP) - PSUSA/00001696/202011

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Idebenone²⁶ (NAP) - PSUSA/00001721/202009

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Ketotifen²⁷ (NAP) - PSUSA/00001813/202010

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Lidocaine (NAP) - PSUSA/00001861/202009

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Minoxidil²⁸ (NAP) - PSUSA/00002066/202010

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

²⁵ Including all fixed combinations

²⁶ Non-centrally authorised product(s) only

²⁷ Oral formulation(s) only

²⁸ All except topical formulation(s)

6.3.22. Minoxidil²⁹ (NAP) - PSUSA/00002067/202010

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Perindopril (NAP) - PSUSA/00002354/202010

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Polystyrene sulfonate (NAP) - PSUSA/00002472/202010

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Prulifloxacin (NAP) - PSUSA/00002569/202010

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Rubidium (⁸²Rb) chloride (NAP) - PSUSA/00010806/202010

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Salmeterol (NAP) - PSUSA/00002681/202010

Applicant(s): various

PRAC Lead: Annika Folin

²⁹ Topical formulation(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Tetrabenazine (NAP) - PSUSA/00002911/202010

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Triamcinolone³⁰ (NAP) - PSUSA/00010137/202009

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Hydroxycarbamide - SIKLOS (CAP) - EMEA/H/C/000689/LEG 034

Applicant: Addmedica S.A.S.

PRAC Rapporteur: Laurence de Fays

Scope: Review of available data on paediatric patients < 2 years of age and on pregnancy as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001692/202006) adopted by PRAC in January 2021

Action: For adoption of advice to CHMP

6.4.2. Hydroxycarbamide - XROMI (CAP) - EMEA/H/C/004837/LEG 005

Applicant: Nova Laboratories Ireland Limited

PRAC Rapporteur: Laurence de Fays

Scope: Review of available data on paediatric patients < 2 years of age and on pregnancy as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001692/202006) adopted by PRAC in January 2021

Action: For adoption of advice to CHMP

6.4.3. Methotrexate - JYLAMVO (CAP) - EMEA/H/C/003756/LEG 002.1

Applicant: Therakind (Europe) Limited

³⁰ Tablets and injectables only

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 002 [comprehensive review of the value of performing liver biopsies as a diagnostic tool to monitor hepatotoxicity of methotrexate in non-oncologic indications as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002014/201910) adopted in May 2020] as per the request for supplementary information (RSI) adopted in January 2021

Action: For adoption of advice to CHMP

6.4.4. Methotrexate - NORDIMET (CAP) - EMEA/H/C/003983/LEG 003.1

Applicant: Nordic Group B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 003 [comprehensive review of the value of performing liver biopsies as a diagnostic tool to monitor hepatotoxicity of methotrexate in non-oncologic indications as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002014/201910) adopted in May 2020] as per the request for supplementary information (RSI) adopted in January 2021

Action: For adoption of advice to CHMP

6.4.5. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/LEG 008

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Review of cases of rapid correction of hyponatremia and neurological sequelae as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010395/202005) adopted in January 2021

Action: For adoption of advice to CHMP

6.4.6. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/LEG 049.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to LEG 049 [cumulative review of cases of major adverse cardiovascular events (MACE), including fatal cases, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00003085/201912) adopted in July 2020] as per the request for supplementary information (RSI) adopted in January 2021

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Decitabine - DACOGEN (CAP) - EMEA/H/C/002221/II/0044, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 4.6 of the SmPC in order to update information on fertility, pregnancy and lactation as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00009118/202005) adopted in January 2021. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives for Italy in the package leaflet and to include some editorial changes in the product information to align with standard English spelling

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews³¹

6.6.1. Coronavirus (COVID-19) mRNA³² vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.4

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC Assessment Report

6.6.2. Coronavirus (COVID-19) mRNA³³ vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/MEA 011.3

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Fourth 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. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/MEA 014.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second expedited monthly summary safety report for Janssen COVID-19 Vaccine (COVID-19 vaccine (Ad26.COV2-S, recombinant)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

³¹ 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

³² Messenger ribonucleic acid

³³ Messenger ribonucleic acid

6.6.4. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 027.2

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Third expedited monthly summary safety report for Vaxzevria (COVID-19 vaccine (ChAdOx1-S [recombinant])) 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)³⁴

7.1.1. Blinatumomab – BLINCYTO (CAP) - EMEA/H/C/PSA/S/0065.1

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: MAH's response to PSA/S/0065 [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] as per the request for supplementary information (RSI) adopted in February 2021

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

7.1.2. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/PSP/S/0089.1

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to PSP/S/0089 [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)] as per the request for supplementary information (RSI) adopted in February 2021

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

7.1.3. Betibeglogene autotemcel – ZYNTEGLO (CAP) - EMEA/H/C/PSP/S/0090.1

Applicant: Bluebird bio (Netherlands) B.V., ATMP³⁵

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to PSP/S/0090 [protocol for study REG-504: a non-interventional

³⁴ In accordance with Article 107n of Directive 2001/83/EC

³⁵ Advanced therapy medicinal product

post-authorisation safety and efficacy study to further characterise and contextualise the long-term safety and efficacy of Zynteglo (betibeglogene autotemcel) in patients aged 12 years and older with transfusion-dependent β -thalassaemia (TDT) who do not have a $\beta 0 / \beta 0$ genotype] as per the request for supplementary information (RSI) adopted in March 2021

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

7.1.4. Elosulfase alfa – VIMIZIM (CAP) - EMEA/H/C/PSA/S/0062.1

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to PSA/S/0062 [substantial amendment to a protocol previously agreed in the framework of the initial marketing authorisation(s) for a multicentre, multinational, observational Morquio A Registry Study (MARS) to characterise and describe the mucopolysaccharidosis IV type A (MPS IVA) population as a whole, including the heterogeneity, progression, and natural history of MPS IVA and to track the safety and clinical outcomes of patients with MPS IVA patients treated with Vimizim (elosulfase alfa)] as per the request for supplementary information (RSI) adopted in January 2021

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

7.1.5. Valproate (NAP) - EMEA/H/N/PSP/J/0094

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for a joint retrospective study of multiple European data sources characterising neurodevelopmental disorders in children exposed in utero to valproate and/or other antiepileptic drugs with long-term follow-up

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

7.1.6. Vestronidase alfa – MEPSEVII (CAP) - EMEA/H/C/PSA/S/0069

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Eva Segovia

Scope: Substantial amendment to a protocol previously agreed in September 2019 ([PSP/S/0082](#)) for a PASS to obtain long-term data on effectiveness and safety of treatment with Mepsevii (vestronidase alfa) and to characterise the entire mucopolysaccharidosis VII, including variability of clinical manifestation, progression and natural history

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)³⁶

7.2.1. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/MEA 002

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study CBYL719C2404: a non-interventional study of Piqray (alpelisib) in combination with fulvestrant in postmenopausal women and men with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative, locally advanced or metastatic breast cancer with a PIK3CA mutation in the real-world setting in European countries, as per the outcome of variation II/001 finalised in March 2021. The safety concerns addressed are hyperglycaemia and osteonecrosis of the jaw

Action: For adoption of advice to CHMP

7.2.2. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 002

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-9046: a non-interventional PASS of filgotinib in the treatment of patients with moderate to severe active rheumatoid within the German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) [final report expected in Q4 2029]

Action: For adoption of advice to CHMP

7.2.3. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 003

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-9047: a non-interventional PASS of filgotinib in the treatment of patients with moderate to severe active rheumatoid arthritis within the Anti-Rheumatic Treatment in Sweden (ARTIS) register [final report expected in Q2 2030]

Action: For adoption of advice to CHMP

7.2.4. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 004

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-9048: a non-interventional PASS of filgotinib in the treatment of patients with moderate to severe active rheumatoid arthritis within the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA) [final report expected in Q3 2030]

³⁶ 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

Action: For adoption of advice to CHMP

7.2.5. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 005

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-5882: a non-interventional PASS of filgotinib in the treatment of patients with moderate to severe active rheumatoid arthritis within the Spanish Registry of Adverse Events of Biological Therapies in Rheumatoid Diseases (BIOBADASER) [final report expected in Q3 2030]

Action: For adoption of advice to CHMP

7.2.6. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 006

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-5883: a non-interventional PASS of filgotinib in the treatment of patients with moderate to severe active rheumatoid arthritis within the Danish Nationwide Clinical Register for Patients with Rheumatoid Arthritis (DANBIO) [final report expected in Q2 2030]

Action: For adoption of advice to CHMP

7.2.7. Inclisiran - LEQVIO (CAP) - EMEA/H/C/005333/MEA 004

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Protocol for study CKJX839A12011: a non-interventional PASS to estimate the proportion of major congenital malformations among pregnancies exposed to inclisiran during pregnancy reported to Novartis amongst (i) live births and (ii) live births plus still births plus termination of pregnancy for foetal anomaly (TOPFA) - Inclisiran pregnancy outcomes intensive monitoring (PRIM) (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.2.8. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 020.3

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: MAH's response to MEA 020.2 [protocol for study CT-P13 4.8: an observational, prospective cohort study to evaluate the safety of Remsima (infliximab) subcutaneous in patients with rheumatoid arthritis (RA)] as per the request for supplementary information (RSI) adopted in January 2021

Action: For adoption of advice to CHMP

7.2.9. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 021.1

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: MAH's response to MEA 021 [protocol for study CT-P13 4.9: an observational, prospective cohort study to evaluate safety of Remsima (infliximab) subcutaneous in patients with ankylosing spondylitis, psoriatic arthritis, and psoriasis] as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

7.2.10. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/MEA 002.1

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002 [protocol for study VX20-445-120: a five year-registry based study to assess real-world effects and utilisation patterns of elexacaftor/tezacaftor/ivacaftor combination therapy (ELX/TEZ/IVA) in patients with cystic fibrosis (CF)] as per the request for supplementary information (RSI) adopted in January 2021

Action: For adoption of advice to CHMP

7.2.11. Lumasiran - OXLUMO (CAP) - EMEA/H/C/005040/MEA 002

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study ALN-GO1-007 an observational PASS to characterise the long-term real-world safety of lumasiran in patients with primary hyperoxaluria type 1 (PH1) (from initial opinion/marketing authorisation (MA))

Action: For adoption of advice to CHMP

7.2.12. Lusutrombopag - MULPLEO (CAP) - EMEA/H/C/004720/MEA 002.2

Applicant: Shionogi B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 002.1 [protocol for study VV-REG-090246: a PASS exploring the hepatic safety of lusutrombopag Shionogi in patients with Child-Pugh class C liver disease (from initial opinion/marketing authorisation (MA)) [final study report expected in December 2025]] as per the request for supplementary information (RSI) adopted in January 2021

Action: For adoption of advice to CHMP

7.2.13. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/MEA 002.3

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Amendment to a protocol previously agreed in March 2019 for study 3000-04-001: a non-interventional PASS to evaluate the risks of myelodysplastic syndrome (MDS)/ acute myeloid leukaemia (AML) and secondary primary malignancies (SPM) in adult patients with platinum-sensitive, relapsed, high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer receiving maintenance treatment with Zejula (niraparib)]

Action: For adoption of advice to CHMP

7.2.14. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 004.9

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Amendment to a protocol previously agreed in September 2019 together with a feasibility assessment for study CLCZ696B2015 (PASS 3) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of Entresto/Neparvis (sacubitril/valsartan) [final study report expected in December 2022]

Action: For adoption of advice to CHMP

7.2.15. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/MEA 003.6

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Amendment to a protocol previously agreed in September 2019 together with a feasibility assessment for study CLCZ696B2015 (PASS 3) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of Entresto/Neparvis (sacubitril/valsartan) [final study report expected in December 2022]

Action: For adoption of advice to CHMP

7.2.16. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 003.3

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Amendment to a protocol previously agreed in May 2017 for study AC-065A403: a PASS to evaluate risk minimisation measures for mEDication errors with Uptravi (selexipag) during the titration phase in patients with pulmonary arterial hypertension (PAH) in Clinical prAcTicE (EDUCATE)

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)³⁷

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)³⁸

7.4.1. 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

7.4.2. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0039, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Submission of the final report from study 20180138 (listed as a category 3 study in the RMP): a long-term follow-up of adult Philadelphia chromosome-negative acute lymphoblastic leukaemia (ALL) relapsed refractory patients enrolled in study 00103311: a phase 3, randomized, open label study investigating the efficacy of the blinatumomab versus standard of care chemotherapy in adult subjects with relapsed/refractory B-precursor ALL (TOWER Study), in order to update the overall survival (OS) Kaplan-Meier probability estimates

Action: For adoption of PRAC Assessment Report

7.4.3. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0099

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study RA0020 (listed as a category 3 study in the RMP): a nationwide prospective observational cohort study in Germany on the long-

³⁷ In accordance with Article 107p-q of Directive 2001/83/EC

³⁸ 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

term safety and effectiveness of biologic disease-modifying antirheumatic drugs (bDMARDs) in rheumatoid arthritis (RA). In addition, this submission includes a safety analysis across the 4 completed RA registries (Antirheumatic Therapies in Sweden (ARTIS), National Data Bank (NDB), British Society for Rheumatology Biologics Register (BSRBR) and Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)) as per the conclusions of variations II/0072, II/0081, and II/0087 finalised in January 2019, September 2019 and June 2020 respectively. The RMP (version 19.0) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

7.4.4. [Brolucizumab - BEOVU \(CAP\) - EMEA/H/C/004913/II/0008](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.8 of the SmPC in order to include the description of intraocular inflammation, based on the final results from a non-interventional retrospective real-world evidence study conducted in patients with neovascular (wet) age-related macular degeneration (nAMD) to better understand the incidence of adverse events/safety signal after initiating treatment with brolucizumab for up to 6 months

Action: For adoption of PRAC Assessment Report

7.4.5. [Dabigatran etexilate - PRADAXA \(CAP\) - EMEA/H/C/000829/II/0126/G](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped variation consisting of: 1) submission of the final report from drug utilisation study 1160.129 (GLORIA AF): a three-phase, international, multicentre, prospective, observational registry programme in patients with newly diagnosed non-valvular atrial fibrillation (NV AF) at risk for stroke in order to investigate patient characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients globally and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke; 2) submission of the final report from drug utilisation study 1160.136 (EU GLORIA AF) (listed as a category 3 study in the RMP): a three-phase, international, multicentre, prospective, observational registry programme in patients with newly diagnosed non-valvular atrial fibrillation (NV AF) at risk for stroke in order to investigate patient characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients from participating countries in EU/EEA Member States and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke. The RMP (version 39) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. [Dibotermin alfa - INDUCTOS \(CAP\) - EMEA/H/C/000408/II/0100](#)

Applicant: Medtronic BioPharma B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study report from study EUPAS32916 (listed as category 3 study in the RMP): an observational study to evaluate the effectiveness of additional risk minimisation measures for InductOs (dibotermin alfa). The product information and the RMP (version 2.1) are updated accordingly. In addition, the MAH took the opportunity to submit study protocol for study EUPAS32916 as suggested by PRAC

Action: For adoption of PRAC Assessment Report

7.4.7. [Herpes zoster vaccine \(recombinant, adjuvanted\) - SHINGRIX \(CAP\) - EMEA/H/C/004336/II/0045](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Update of section 4.4 of the SmPC in order to add a new warning on an increased risk of Guillain-Barré Syndrome (GBS) after vaccination with Shingrix (herpes zoster vaccine) observed in a post-marketing observational study in individuals aged 65 years or older. The RMP (version 5.1) is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes to the SmPC and to update the list of local representatives in the package leaflet

Action: For adoption of PRAC Assessment Report

7.4.8. [Human normal immunoglobulin - HYQVIA \(CAP\) - EMEA/H/C/002491/II/0070/G](#)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) update of section 4.6 of the SmPC in order to update information on pregnancy and breast-feeding based on the final results from study 161301 (listed as a category 3 study in the RMP): an observational pregnancy registry study to collect long-term safety data from women treated with HyQvia (human normal immunoglobulin). The package leaflet and the RMP (version 12,0) are updated accordingly. In addition, the MAH took the opportunity to implement minor corrections and editorial changes to the SmPC; 2) submission of an updated RMP (version 12.0) to update the educational material (additional risk minimisation measures) as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001633/202005)

Action: For adoption of PRAC Assessment Report

7.4.9. [Lomitapide - LOJUXTA \(CAP\) - EMEA/H/C/002578/II/0047](#)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Introduction of an enhanced pharmacovigilance system to evaluate the occurrence and outcomes of pregnancy in females of reproductive potential treated with lomitapide who decide to continue the pregnancy following advice from a teratologist/clinician, replacing the currently agreed pregnancy exposure register (PER) (listed as part of Annex II-E on 'specific

obligation to complete post-authorisation measures for the marketing authorisation under exceptional circumstances'). The RMP (version 6.5) is updated accordingly. In addition, the MAH took the opportunity to introduce minor administrative changes

Action: For adoption of PRAC Assessment Report

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

7.5.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 048.9

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual update report on recruitment for study IM101240 (listed as a category 3 study in the RMP): an observational registry of abatacept in patients with juvenile idiopathic arthritis (JIA registry) to explore the long-term safety of abatacept treatment for JIA in routine clinical practice by quantifying the incidence rates of serious infections, autoimmune disorders and malignancies [final registry report expected by 2029]

Action: For adoption of advice to CHMP

7.5.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 065.11

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Twelfth interim annual report for study P10-023, a psoriasis patient registry: a 10-year, post-marketing observational study to assess the long term safety of Humira (adalimumab) in adult patients with chronic plaque psoriasis (PS) [final registry report expected in February 2023]

Action: For adoption of advice to CHMP

7.5.3. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/MEA 050.2

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: First interim report for study C18477-ONC-50025: a post-authorisation long term safety cohort study in acute promyelocytic leukaemia (APL) patients treated with Trisenox (arsenic trioxide) to assess the long-term safety of all-trans retinoic acid (ATRA) + arsenic trioxide (ATO) in newly diagnosed low to intermediate risk APL patients in a real-world clinical practice setting [final report expected in 2Q 2023]

Action: For adoption of advice to CHMP

7.5.4. Autologous CD34⁺ enriched cell fraction that contains CD34⁺ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) cDNA sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/ANX 004.3

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP³⁹

PRAC Rapporteur: Menno van der Elst

Scope: Second interim report for study GSK2696273 – an adenosine deaminase severe combined immunodeficiency (ADA-SCID) registry for patients treated with Strimvelis gene therapy: a long-term prospective, non-interventional follow-up of safety and effectiveness

Action: For adoption of advice to CAT and CHMP

7.5.5. Coronavirus (COVID-19) mRNA⁴⁰ vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/MEA 003.1

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Interim report for an enhanced pharmacovigilance study (listed as a category 3 study in the RMP) to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals - post authorisation safety of SARS-CoV-2 mRNA-1273 vaccine in the US [final clinical study report (CSR) expected in June 2023] (from initial opinion/marketing authorisation (MA))

Action: For adoption of advice to CHMP

7.5.6. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 007.10

Applicant: Hexal AG

PRAC Rapporteur: Menno van der Elst

Scope: Tenth annual report for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation [final clinical study report (CSR) expected in December 2024]] together with MAH's response to MEA 007.8 as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.5.7. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.10

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Tenth annual report for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation [final

³⁹ Advanced therapy medicinal product

⁴⁰ Messenger ribonucleic acid

clinical study report (CSR) expected in December 2024]] together with MAH's response to MEA 007.8 as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.5.8. Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/MEA 041.4

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Fifth interim report for Insuman (insulin human) implantable registry HUBIN-C-06380: a European observational cohort of patients with type 1 diabetes treated via intraperitoneal route with Insuman implantable 400 IU/mL (insulin human) in Medtronic MiniMed implantable pump

Action: For adoption of advice to CHMP

7.5.9. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/ANX 003.6

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to ANX 003.5 [fourth annual report for study VX14 809 108 (listed as a category 1 study in Annex II and the RMP): 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] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CHMP

7.5.10. Mercaptamine - CYSTADROPS (CAP) - EMEA/H/C/003769/MEA 001.3

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: First annual report for study CYT-DS-001 (listed as a category 3 study in the RMP): an open-label longitudinal PASS to assess the safety of Cystadrops (mercaptamine) in paediatric and adult cystinosis patients in long term use

Action: For adoption of advice to CHMP

7.5.11. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 002.6

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Fourth interim results for study CLCZ696B2014 (PASS 1) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to characterise the risk of angioedema and other specific safety events of interest in association with the use of Entresto/Neparvis (sacubitril/valsartan) in adult patients with

heart failure [final report expected in Q4/2022]

Action: For adoption of advice to CHMP

7.5.12. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/MEA 002.3

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Fourth interim results for study CLCZ696B2014 (PASS 1) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to characterise the risk of angioedema and other specific safety events of interest in association with the use of Entresto/Neparvis (sacubitril/valsartan) in adult patients with heart failure [final report expected in Q4/2022]

Action: For adoption of advice to CHMP

7.5.13. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/MEA 002.5

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Second interim report for safety surveillance programme using existing EU rheumatoid arthritis (RA) registries conducted in four countries: Germany (German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) (OBS15180)), Spain (Spanish Registry for Adverse Events for Biological Therapy in Rheumatic Diseases (BIOBASASER) (6R88-RA-1720)), Sweden (Register for Antirheumatic Therapies in Sweden (ARTIS) (OBS15220)) and UK (British Society for Rheumatology Biologicals Register (BSRBR) (6R88-RA-1634))

Action: For adoption of advice to CHMP

7.5.14. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 001.6

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Fourth annual interim report for PASS AC-065A401 (EXPOSURE): an observational cohort study of pulmonary arterial hypertension (PAH) patients newly treated with either Uptravi (selexipag) or any other PAH-specific therapy in routine clinical practice [final study report expected in 2023]

Action: For adoption of advice to CHMP

7.5.15. Tisagenlecleucel - KYMRIA (CAP) - EMEA/H/C/004090/ANX 003.5

Applicant: Novartis Europharm Limited, ATMP⁴¹

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Third semi-annual report for a study based on disease registry CCTL019B2401

⁴¹ Advanced therapy medicinal product

(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] (European Society for Blood and Marrow Transplant (EBMT) data only)

Action: For adoption of advice to CAT and CHMP

7.5.16. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 008.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: First interim study report for study A3921312 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA)

Action: For adoption of advice to CHMP

7.5.17. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 009.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: First interim study report for study A3921314 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Swedish (ARTIS) register

Action: For adoption of advice to CHMP

7.5.18. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 010.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: First interim study report for study A3921316 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Spanish registry of adverse events of biological therapies and biosimilars in rheumatoid diseases (BIOBADASER)

Action: For adoption of advice to CHMP

7.5.19. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 011.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: First interim study report for study A3921317 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)

Action: For adoption of advice to CHMP

7.5.20. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 018.5

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Fifth yearly progress report for study PGL14-001: a prospective, multinational, multicentre, non-interventional study to evaluate the long-term safety of Esmya (ulipristal acetate) in particular the endometrial safety and the current prescription and management patterns of Esmya (ulipristal acetate) in a long-term treatment setting [final clinical study report (CSR) expected in 2023]

Action: For adoption of advice to CHMP

7.5.21. Umeclidinium - ROLUFTA ELLIPTA (CAP) - EMEA/H/C/004654/ANX 003

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Interim report for study 201038 (EU PASS 10316): non-interventional post-authorisation safety (PAS) observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients with umeclidinium/vilanterol (UMEC/VI) combination, or inhaled UMEC versus tiotropium

Action: For adoption of advice to CHMP

7.5.22. Umeclidinium, vilanterol - ANORO ELLIPTA (CAP) - EMEA/H/C/002751/ANX 001.2

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Interim report for study 201038 (EU PASS 10316): non-interventional post-authorisation safety (PAS) observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients with umeclidinium/vilanterol (UMEC/VI) combination, or inhaled UMEC versus tiotropium

Action: For adoption of advice to CHMP

7.5.23. Umeclidinium, vilanterol - LAVENTAIR ELLIPTA (CAP) - EMEA/H/C/003754/ANX 001.2

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Interim report for study 201038 (EU PASS 10316): non-interventional post-authorisation safety (PAS) observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients with umeclidinium/vilanterol (UMEC/VI) combination, or inhaled UMEC versus tiotropium

Action: For adoption of advice to CHMP

7.5.24. Umeclidinium bromide - INCRUSE ELLIPTA (CAP) - EMEA/H/C/002809/ANX 001.2

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Interim report for study 201038 (EU PASS 10316): non-interventional post-authorisation safety (PAS) observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients with umeclidinium/vilanterol (UMEC/VI) combination, or inhaled UMEC versus tiotropium

Action: For adoption of advice to CHMP

7.5.25. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.11

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Third interval safety registry for study CNTO1275PSO4056: an observational PASS of ustekinumab in the treatment of paediatric patients aged 12 years and older with moderate to severe plaque psoriasis (adolescent registry)

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Avatrombopag - DOPTelet (CAP) - EMEA/H/C/004722/MEA 002.3

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002.2 [feasibility assessment for study AVA-CLD-402: evaluation of the feasibility of conducting a PASS of Doptelet (avatrombopag) in patients with severe chronic liver disease (CLD) and of the use of potential European electronic health care databases] as per the request for supplementary information (RSI) adopted in January 2021

Action: For adoption of advice to CHMP

7.6.2. Ciclosporin - VERKAZIA (CAP) - EMEA/H/C/004411/MEA 001.3

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Feasibility assessment report for study Oxon 114-59 (version 3.0): a feasibility study for a case-control study linked to existing cancer registries to understand the data sources and analytic methods available to quantify the risk of periocular skin cancer, conjunctival or corneal neoplasia in children treated with Verkazia (ciclosporin)

Action: For adoption of advice to CHMP

7.6.3. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/LEG 028.3

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Fourth six-monthly update on the development of the child-resistant multi-dose nasal spray DoseGuard as requested in the conclusions of procedure R/0049 finalised in April 2019

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. Clofarabine - EVOLTRA (CAP) - EMEA/H/C/000613/S/0072 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. [Velmanase alfa - LAMZEDE \(CAP\) - EMEA/H/C/003922/S/0019 \(without RMP\)](#)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

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. [Bulevirtide - HEPCLUDEX \(CAP\) - EMEA/H/C/004854/R/0003 \(without RMP\)](#)

Applicant: MYR GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. [Crizanlizumab - ADAKVEO \(CAP\) - EMEA/H/C/004874/R/0003 \(without RMP\)](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Laurence de Fays

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. [Larotrectinib - VITRAKVI \(CAP\) - EMEA/H/C/004919/R/0014 \(without RMP\)](#)

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. **Renewals of the marketing authorisation**

8.3.1. [Baricitinib - OLUMIANT \(CAP\) - EMEA/H/C/004085/R/0025 \(without RMP\)](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Darunavir - DARUNAVIR MYLAN (CAP) - EMEA/H/C/004068/R/0014 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Edotreotide - SOMAKIT TOC (CAP) - EMEA/H/C/004140/R/0019 (with RMP)

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Ronan Grimes

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Emtricitabine, tenofovir disoproxil - EMTRICITABINE/TENOFOVIR DISOPROXIL KRKA (CAP) - EMEA/H/C/004215/R/0018 (without RMP)

Applicant: KRKA, d.d., Novo mesto

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Emtricitabine, tenofovir disoproxil - EMTRICITABINE/TENOFOVIR DISOPROXIL MYLAN (CAP) - EMEA/H/C/004050/R/0016 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Enoxaparin sodium - INHIXA (CAP) - EMEA/H/C/004264/R/0076 (with RMP)

Applicant: Techdow Pharma Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Etelcalcetide - PARSABIV (CAP) - EMEA/H/C/003995/R/0017 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. [Insulin aspart - FIASP \(CAP\) - EMEA/H/C/004046/R/0028 \(with RMP\)](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. [Lonococog alfa - AFSTYLA \(CAP\) - EMEA/H/C/004075/R/0037 \(with RMP\)](#)

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. [Sildenafil - GRANPIDAM \(CAP\) - EMEA/H/C/004289/R/0009 \(without RMP\)](#)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. [Tenofovir disoproxil - TENOFOVIR DISOPROXIL MYLAN \(CAP\) - EMEA/H/C/004049/R/0022 \(without RMP\)](#)

Applicant: Mylan S.A.S

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. [Teriparatide - MOVYMIA \(CAP\) - EMEA/H/C/004368/R/0024 \(with RMP\)](#)

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Ronan Grimes

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Teriparatide - TERROSA (CAP) - EMEA/H/C/003916/R/0020 (with RMP)

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ronan Grimes

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

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

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

Information related to this section cannot be released at the present time as it is deemed to

contain commercially confidential information.

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Levothyroxine (NAP) - DE/H/XXXX/WS/674

Applicant: Berlin Chemie AG (Menarini Group) (Berlthyrox)

PRAC Lead: Martin Huber

Scope: PRAC consultation on the need for a communication strategy in the context of a worksharing quality variation for Berlthyrox (levothyroxine) on request of Germany

Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Methotrexate⁴² (NAP) - DE/H/PSUFU/00002014/201910

Applicant(s): Addenda Pharma, Especialidades Farmacéuticas Centrum S.A., Gebro Pharma, medac, Morningside Healthcare Limited, Mylan, Nordic Group, Orion Pharma, Pfizer, Remedica, Rompharm, Sandoz, Teva

PRAC Lead: Martin Huber

Scope: PRAC further consultation on a PSUR follow-up (PSU FU) procedure evaluating comprehensive reviews of the value of performing liver biopsies as a diagnostic tool to monitor hepatotoxicity of methotrexate in non-oncologic indications, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure (PSUSA/00002014/201910) concluded in May 2020, on request of Germany

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. Mandate of PRAC Chairperson

Action: For discussion

⁴² In non-oncology indication(s)

12.2. Coordination with EMA Scientific Committees or CMDh-v

- 12.2.1. Committee for Medicinal Products for Human Use (CHMP)-PRAC collaboration group – safety specification assessment responsibilities for generic medicinal products in initial marketing authorisation applications
-

Action: For discussion

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

None

12.4. Cooperation within the EU regulatory network

- 12.4.1. Coronavirus (COVID-19) pandemic - update
-

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

- 12.9.1. Pharmacovigilance systems and their quality systems
-

None

- 12.9.2. Pharmacovigilance inspections
-

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC Lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC Lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. Coronavirus (COVID-19) pandemic - National competent authorities (NCA) prioritisation of individual case safety report (ICSRs) submissions to EudraVigilance - Note for guidance

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.14.3. Coronavirus (COVID-19) pandemic - coreRMP19: variants guidance for RMP requirements, traceability and others

Action: For discussion

12.14.4. Good pharmacovigilance practice (GVP) module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' – revision 3 and addendum II on principles and methods to evaluate the effectiveness of risk minimisation measures (RMM)

PRAC Lead: Sabine Straus

Action: For discussion

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Good Pharmacovigilance Practice (GVP) – mid-year update

PRAC Lead: Sabine Straus

Action: For discussion

12.20.2. Research and innovation workstream

Action: For discussion

12.20.3. Titanium dioxide (E171) – European Commission (EC) letter

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/