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Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 08-11 June 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

08 June 2020, 10:30 – 19:30, via teleconference

09 June 2020, 08:30 – 19:30, via teleconference

10 June 2020, 08:30 – 19:30, via teleconference

11 June 2020, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

25 June 2020, 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 08-11 June 2020. See June 2020 PRAC minutes (to be published post July 2020 PRAC meeting).

1.2. Agenda of the meeting on 08-11 June 2020

Action: For adoption

1.3. Minutes of the previous meeting on 11-14 May 2020

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. Ulipristal acetate – ESMYA (CAP); NAP - EMEA/H/A-31/1496

Applicant(s): Gedeon Richter Plc.; various

PRAC Rapporteur: Annika Folin; 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 31 of Directive 2001/83/EC, based on

pharmacovigilance data

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

3.3. Procedures for finalisation

None

3.4. Re-examination procedures¹

None

3.5. Others

None

4. Signals assessment and prioritisation²

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Capecitabine – CAPECITABINE ACCORD (CAP), CAPECITABINE MEDAC (CAP), CAPECITABINE TEVA (CAP), ECANSYA (CAP), XELODA (CAP); NAP

Applicant(s): Accord Healthcare S.L.U. (Capecitabine Accord), Krka, d.d., Novo mesto (Ecansya), Medac Gesellschaft für klinische Spezialpräparate mbH (Capecitabine Medac); Roche Registration GmbH (Xeloda), Teva B.V. (Capecitabine Teva)

PRAC Rapporteur: To be appointed

Scope: Signal of anaphylactic reaction

Action: For adoption of PRAC recommendation

EPITT 19561 – New signal

Lead Member State(s): DE

4.1.2. Cefepime (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

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

Action: For adoption of PRAC recommendation

EPITT 17866 – New signal

Lead Member State(s): PT

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

² Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

4.1.3. Chloroquine (NAP); hydroxychloroquine (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of psychiatric disorders

Action: For adoption of PRAC recommendation

EPITT 19572 – New signal

Lead Member State(s): DK, SE

4.1.4. Cladribine - MAVENCLAD (CAP)

Applicant(s): Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of seizure

Action: For adoption of PRAC recommendation

EPITT 19573 – New signal

Lead Member State(s): PT

4.1.5. Nivolumab – OPDIVO (CAP)

Applicant(s): Bristol-Myers Squibb Pharma

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of eosinophilic fasciitis

Action: For adoption of PRAC recommendation

EPITT 19567 – New signal

Lead Member State(s): DE

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Amitriptyline (NAP); bupropion (NAP); citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); mirtazapine (NAP); paroxetine (NAP); sertraline (NAP); trazodone (NAP); venlafaxine (NAP)

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of post-partum haemorrhage

Action: For adoption of PRAC recommendation

EPITT 19552 – Follow-up to March 2020

4.3.2. Desogestrel (NAP)

Applicant(s): various

PRAC Rapporteur: Annika Folin

Scope: Signal of suppressed lactation

Action: For adoption of PRAC recommendation

EPITT 19504 - Follow-up to January 2020

4.3.3. Macrogol 3350³ 4 (NAP); macrogol 4000⁵ 6 (NAP)

Applicant(s): various

PRAC Rapporteur: Ilaria Baldelli

Scope: Signal of colitis ischaemic

Action: For adoption of PRAC recommendation

EPITT 19517 – Follow-up to February 2020

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Abiraterone acetate - ZYTIGA (CAP) - EMEA/H/C/002321/II/0061

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to add a warning on hypoglycaemia based on the final signal recommendation adopted in January 2020 (EPITT 19445) on interaction between abiraterone and sulphonylureas. The package leaflet is updated accordingly. The MAH took the opportunity to introduce some minor updates to Annex II of the product information

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Arachis hypogaea allergens, arachis hypogaea allergens - EMEA/H/C/004917

Scope: Oral immunotherapy (OIT) for patients aged 4 to 17 years with a confirmed diagnosis of peanut allergy

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

³ With or without electrolytes

⁴ And combination(s)

⁵ With or without electrolytes

⁶ And combination(s)

5.1.2. [Bupivacaine - EMEA/H/C/004586](#)

Scope: Management of prolonged acute pain and reduction in need for opioids in adults compared to immediate-release bupivacaine

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

5.1.3. [Dasatinib - EMEA/H/C/005446](#)

Scope: Treatment of leukaemia

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

5.1.4. [Dasatinib - EMEA/H/C/005317](#)

Scope: Treatment of leukaemia

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

5.1.5. [Dostarlimab - EMEA/H/C/005204](#)

Scope (accelerated assessment): Treatment of deficient mismatch repair (dMMR), microsatellite instability-high (MSI-H) endometrial cancer (EC)

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

5.1.6. [Fenfluramine - EMEA/H/C/003933, Orphan](#)

Applicant: Zogenix GmbH

Scope: Treatment of seizures associated with Dravet syndrome in children aged 2 years to 17 years and adults

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

5.1.7. [Lenalidomide - EMEA/H/C/005306](#)

Scope: Treatment of multiple myeloma

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

5.1.8. [Pegfilgrastim - EMEA/H/C/005085](#)

Scope: Treatment of neutropenia

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

5.1.9. [Sodium thiosulfate - EMEA/H/C/005130](#)

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

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

5.1.10. Somapacitan – EMEA/H/C/005030, Orphan

Applicant: Novo Nordisk A/S

Scope: Replacement of endogenous growth hormone (GH) in adults with growth hormone deficiency (AGHD)

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. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0033, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Submission of an updated RMP (version 11) in line with revision 2 of GVP module V on 'Risk management systems'. The protocol for study 20150136 (listed as a category 1 in the RMP/Annex II): an observational study of blinatumomab safety and effectiveness, utilisation, and treatment practices is updated and the enrolment period extended by 1 year. As a consequence, the milestones in the RMP are updated accordingly. In addition, the RMP includes a proposed update to the milestone of study 20180138 (listed as a category 3 study in the RMP): long-term follow-up of patients enrolled in TOWER study: a phase 3, randomized, open label study investigating the efficacy of the bispecific T-cell engager (BiTE) antibody blinatumomab versus standard of care chemotherapy in adult subjects with relapsed/refractory B-precursor acute lymphoblastic leukaemia (ALL)

Action: For adoption of PRAC Assessment Report

5.2.2. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/WS1747/0231; LIFMIOR⁷ - EMEA/H/C/004167/WS1747/0025

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Submission of an updated RMP (version 7.0) to revise the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and revision 2.0.1 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to implement the outcomes of variation WS/1270 adopted in January 2019 and periodic single assessment procedure (PSUSA) PSUSA/001295/201902 adopted in September 2019 as requested by PRAC/CHMP in order to remove or consolidate several risks. Finally, the MAH removed the addendum to RMP (version 6.3), introduced some clinical and post-marketing data updates and reflected the completion of post-authorisation studies

Action: For adoption of PRAC Assessment Report

5.2.3. Filgrastim - GRASTOFIL (CAP) - EMEA/H/C/002150/II/0030

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Kirsti Villikka

⁷ Marketing authorisation(s) cessation dated 16 February 2020

Scope: Submission of an updated RMP (version 6.0) in order to update the safety concerns and additional pharmacovigilance activities by removing the Severe Chronic Neutropenia International Registry (SCNIR) and the European Society for Blood and Marrow Transplant (EBMT) registries following the conclusion of the SCNIR and EBMT combined analysis report in line with the latest approved RMP (version 4.0) for Accofil (filgrastim) finalised within procedure II/037 concluded in October 2019

Action: For adoption of PRAC Assessment Report

5.2.4. [Human coagulation factor VIII, human von willebrand factor - VONCENTO \(CAP\) - EMEA/H/C/002493/II/0042](#)

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 7) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and reflect the completion of study CSLCT-BIO-12-83: a post-marketing study (PMS) to collect long-term data on the haemostatic efficacy of human coagulation factor VIII/von Willebrand factor (FVIII/VWF) complex in patients with von Willebrand disease (VWD) who require a VWF product to control a bleeding event or as prophylaxis therapy. In addition, the RMP is updated to request a waiver to study Biostate_4001 (listed as a category 3 study in the RMP): a low-interventional multicentre PASS for Vocento (FVIII/VWF) for routine prophylaxis, treatment of bleeding events and/or surgery in male patients with haemophilia A due to feasibility reasons

Action: For adoption of PRAC Assessment Report

5.2.5. [Ibrutinib - IMBRUVICA \(CAP\) - EMEA/H/C/003791/II/0061, Orphan](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Submission of an updated RMP (version 16.2) in order to introduce changes to safety concerns following the conclusions of renewal procedure R/049 finalised in April 2019. The MAH took the opportunity to include additional changes related to two post-authorisation measures, namely the postponement of the completion date of study PCI-32765MCL3002 (listed as a category 3 study in the RMP): a randomized, double-blind, placebo-controlled phase 3 study of the Bruton's tyrosine kinase (BTK) inhibitor, PCI-32765 (ibrutinib), in combination with bendamustine and rituximab (BR) in subjects with newly diagnosed mantle cell lymphoma and the removal of study 54179060CLL1017 on DDI in line with the conclusions of variation II/058 finalised in April 2020

Action: For adoption of PRAC Assessment Report

5.2.6. [Ixazomib - NINLARO \(CAP\) - EMEA/H/C/003844/II/0019/G, Orphan](#)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of: 1) submission of the final report from study NSMM-5001 (listed as a specific obligation (SOB) in Annex II-E on 'Specific obligation to

complete post-authorisation measures for the conditional marketing authorisation): a global, prospective, non-interventional, observational efficacy study in multiple myeloma patients. Annex II and the RMP (version 5.0) are updated accordingly; 2) submission of an updated RMP (version 5.0) in order to extend the due date of post-authorisation efficacy study (PAES) C16010 (listed in Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product': provision of an interim report of overall survival (OS) at the time of the third interim analysis and provision of a final report for the final analysis of OS from the phase 3, randomized, double-blind study C16010 in adult patients with relapsed and/or refractory multiple myeloma. The MAH took the opportunity to correct a typographical error in Annex II

Action: For adoption of PRAC Assessment Report

5.2.7. [Nilotinib - TASIGNA \(CAP\) - EMEA/H/C/000798/II/0103](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 22.0) to include 'growth retardation' as an important identified risk as per the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002162/201901) finalised in September 2019, and to add study CAMN107A2203: a multicentre, open label, non-controlled phase 2 study to evaluate efficacy and safety of oral nilotinib in paediatric patients with newly diagnosed Philadelphia chromosome positive (Ph+) chronic myelogenous leukaemia (CML) in chronic phase (CP) or with Ph+ CML in CP or accelerated phase (AP) resistant or intolerant to either imatinib or dasatinib as an additional pharmacovigilance activity in relation to the important identified risk of 'growth retardation' to the pharmacovigilance plan. In addition, the additional pharmacovigilance activity of collection of gene signature data in patients who relapse on treatment-free remission (TFR) compared to patients who relapse on treatment is deleted from the RMP in line with the conclusions of MEA 051.1 concluded in October 2019. The MAH took the opportunity to revise the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.8. [Pioglitazone - GLIDIPION \(CAP\) - EMEA/H/C/002558/WS1791/0013](#); [PIOGLITAZONE ACTAVIS \(CAP\) - EMEA/H/C/002324/WS1791/0014](#); [PIOGLITAZONE TEVA \(CAP\) - EMEA/H/C/002297/WS1791/0023](#); [PIOGLITAZONE TEVA PHARMA \(CAP\) - EMEA/H/C/002410/WS1791/0023](#)

Applicant(s): Actavis Group PTC ehf (Glipidion, Pioglitazone Actavis), Teva B.V. (Pioglitazone Teva, Pioglitazone Teva Pharma)

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of the RMP (version 4.0) in order to amend the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and in line with the RMP of the originator product containing pioglitazone. In addition, the educational pack for healthcare professionals (HCPs) and the prescriber guide are removed as additional risk minimisation measures (aRMMs) in line with the conclusions of the PSUR single assessment (PSUSA) procedure for pioglitazone and pioglitazone/glimepiride (PSUSA/00002417/201807) finalised in March 2019

Action: For adoption of PRAC Assessment Report

5.2.9. Telotristat ethyl - XERMELO (CAP) - EMEA/H/C/003937/II/0021, Orphan

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

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

Action: For adoption of PRAC Assessment Report

5.2.10. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/II/0029

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 14.4) to include dehydration and the pregnancy prevention programme as additional risk minimisation measures (aRMM) in order to align the RMP with Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product'

Action: For adoption of PRAC Assessment Report

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

5.3.1. Albutrepenonacog alfa - IDELVION (CAP) - EMEA/H/C/003955/X/0035, Orphan

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Extension application to add a new strength of 3,500 IU (700 IU/mL) for albutrepenonacog alfa powder and solvent for solution for injection. The RMP (version 3.1) is updated accordingly

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

5.3.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0042

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include in combination with platinum-based chemotherapy first-line treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC). As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 14.0) are updated accordingly

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

5.3.3. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0076

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information based on the final results from study BEL115467 (listed as an imposed PASS in Annex II): a randomized, double-blind, placebo-controlled 52-week study to assess adverse events of special interest in adults with active, autoantibody-positive systemic lupus erythematosus receiving belimumab. The package leaflet is updated accordingly. The RMP (version 36) is updated in accordance and also includes minor updates. In addition, the MAH took the opportunity to introduce minor editorial changes to Annex II and the labelling

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

5.3.4. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0030, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include the treatment of Philadelphia chromosome positive CD19⁸ positive B-cell precursor acute lymphoblastic leukaemia (ALL) in adult and paediatric patients with relapsed or refractory ALL and adult patients in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%. 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 10.0) are updated accordingly

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

5.3.5. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/II/0014

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.4 and 4.8 of the SmPC to reflect a signal of anaphylactic reaction detected in post marketing setting. The package leaflet and the RMP (version 1.2) are updated accordingly. The MAH took the opportunity to introduce minor updates throughout the product information

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

5.3.6. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/II/0010/G, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of an extension of indication to include the treatment of adults with X-linked hypophosphataemia (XLH), and modification of the currently approved indication in children and adolescents, by removing the qualification 'with growing skeletons', in order to include the treatment in all children with radiographic evidence of bone disease. The application provides new week-48 data from study UX023-CL304: a randomized, double-blind, placebo-controlled, phase 3 study with open-label extension to assess the efficacy and safety of burosumab (KRN23) in adults with XLH. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 2.0) are updated in accordance. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

⁸ Cluster of differentiation 19

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

5.3.7. [Certolizumab pegol - CIMZIA \(CAP\) - EMEA/H/C/001037/II/0087](#)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to introduce a change in posology for axial spondyloarthritis (aSpA) and to update the safety and efficacy information based on the results of study AS0005 (C-OPTIMISE) (listed as a category 3 study in the RMP): a multicentre, open-label (part A) followed by a randomised, double-blind, parallel-group, placebo-controlled study (part B) to evaluate maintenance of remission in subjects with active aSpA receiving either certolizumab pegol 200mg once every 2 weeks (q2w) or 200mg once every 4 weeks (q4w) as compared to placebo. The package leaflet and the RMP (version 17.0) are updated accordingly. In addition, the interim study reports for studies AS0006 and AS0007 are submitted to include additional pooled safety data in the SmPC. Study AS0006 is a phase 3, multicentre, randomised, placebo-controlled, double-blind study to evaluate efficacy and safety of certolizumab pegol in subjects with active aSpA without x-ray evidence of ankylosing spondylitis and objective signs of inflammation. Study AS0007 is a multicentre, open-label study to assess the effects of certolizumab pegol on the reduction of anterior uveitis flares in aSpA subjects with a history of anterior uveitis (C-VIEW)

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

5.3.8. [Clopidogrel - ISCOVER \(CAP\) - EMEA/H/C/000175/WS1820/0142; PLAVIX \(CAP\) - EMEA/H/C/000174/WS1820/0140](#)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of section 4.2 of the SmPC in order to add 600 mg as an alternative loading dose to the existing 300 mg to be used at initiation of treatment in the indication of secondary prevention of atherothrombotic events in adult patients suffering from acute coronary syndrome. This update is based on a bibliographic review of published studies. The package leaflet and the RMP (version 2.0) are updated accordingly

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

5.3.9. [Dapagliflozin - EDISTRIDE \(CAP\) - EMEA/H/C/004161/WS1737/0034; FORXIGA \(CAP\) - EMEA/H/C/002322/WS1737/0053](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to add a new indication for the treatment of symptomatic heart failure with reduced ejection fraction in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and labelling are updated in accordance. The RMP (version 18) is updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1). Finally, the MAH took the opportunity to introduce an editorial change in the product information

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

5.3.10. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0039, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of section 5.1 of the SmPC in order to amend information regarding immunogenicity following completion of post-authorisation commitments in variation II/030 (finalised in December 2019), variation II/032 (finalised in April 2020) on re-analysis of all anti-daratumumab antibodies (ADA) samples taken from previously submitted clinical studies, namely: 1) study MMY1001: an open-label, multicentre, phase 1b study of JNJ-54767414 (daratumumab) in combination with backbone regimens for the treatment of subjects with multiple myeloma; 2) study MMY3003: a phase 3, randomised trial comparing daratumumab, lenalidomide, and dexamethasone vs lenalidomide-dexamethasone in subjects with relapsed or refractory multiple myeloma; 3) study MMY3004: a phase 3, randomised trial comparing daratumumab, bortezomib, and dexamethasone vs bortezomib and dexamethasone in subjects with relapsed or refractory multiple myeloma; 4) study SMM2001: a randomised phase 2 trial to evaluate 3 daratumumab dose schedules in smoldering multiple myeloma; 5) study MMY1004: an open-label, multicentre, dose escalation phase 1b study to assess the safety and pharmacokinetics of subcutaneous delivery of daratumumab with the addition of recombinant human hyaluronidase (rHuPH20) for the treatment of subjects with relapsed or refractory multiple myeloma; 6) study MMY1008: a phase 1 study of subcutaneous delivery of JNJ-54767414 (daratumumab) in Japanese participants with relapsed or refractory multiple myeloma; 7) study MMY2040: a multicentre phase 2 study to evaluate subcutaneous daratumumab in combination with standard multiple myeloma treatment regimens; 8) study MMY3012: a phase 3 randomized, multicentre study of subcutaneous vs. intravenous administration of daratumumab in subjects with relapsed or refractory multiple myeloma; using the enhanced DT method (previously developed as a result of MEA 005). As a result, immunogenicity is removed from the RMP as an important potential risk considering the additional pharmacovigilance activity of 'investigation of a new method for detecting antidrug antibodies' as completed. The RMP (version 6.5) is updated accordingly

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

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

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

PRAC Rapporteur: Željana Margan Koletić

Scope: Extension of indication to include treatment of community acquired pneumonia (CAP) for Quofenix (delafloxacin) 450 mg tablets and 300 mg powder for concentrate for solution for infusion. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 2.0) are updated in accordance

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

5.3.12. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA⁹), poliomyelitis (inactivated) and haemophilus type b conjugate vaccine - HEXACIMA

⁹ Ribosomal deoxyribonucleic acid

Applicant(s): Sanofi Pasteur (Hexaxim, Hexacima), Sanofi Pasteur Europe (Hexyon)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 5.1 of the SmPC in order to revise the existing warning regarding preterm infants and to add new information on immunogenicity in preterm infants and in infants born from women vaccinated during pregnancy based on the final results from study A3L00053-EXT: an observational cohort study conducted by the 'Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute (CEV) of University of Antwerp' with diphtheria, tetanus, pertussis, hepatitis b, poliomyelitis and haemophilus type b conjugate (DTaP-IPV-HB-PRP-T) vaccine, aimed to describe the concentrations of immunoglobulin G (IgG) against different antigens. The RMP (version 12.0) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems'; 2) update of sections 2 and 4.4 of the SmPC in order to add a warning for the following excipients with known effects: phenylalanine, potassium and sodium in line with the Annex to the European Commission (EC) guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. The package leaflet is updated accordingly. In addition, the MAH/Scientific opinion holder (SOH) took the opportunity to introduce editorial changes in sections 4.2, 4.4 and 4.5 of the SmPC and to update the list of local representatives in the package leaflet

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

5.3.13. Eftrenonacog alfa - ALPROLIX (CAP) - EMEA/H/C/004142/II/0029, Orphan

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC to add information on previously untreated patients (PUPs) following the completion of study 998HB303: an open-label, multicentre evaluation of the safety and efficacy of recombinant coagulation factor IX Fc fusion protein (rFIXFc; BIIB029) in the prevention and treatment of bleeding in PUPs with severe haemophilia B (already assessed in procedure P46 006). The package leaflet and the RMP (version 12.1) are updated accordingly

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

5.3.14. Fluticasone furoate, umeclidinium, vilanterol - ELEBRATO ELLIPTA (CAP) - EMEA/H/C/004781/X/0014/G

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Annika Folin

Scope: Grouped application consisting of: 1) extension application to introduce a new strength (184mcg/55mcg/22mcg); 2) extension of indication to add maintenance treatment in adult patients with asthma. As a consequence, sections 2, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and

¹⁰ Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

5.3 of the SmPC are updated. The package leaflet and the RMP (version 2.2) are updated in accordance

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

5.3.15. [Fluticasone furoate, umeclidinium, vilanterol - TEMYBRIC ELLIPTA \(CAP\) - EMEA/H/C/005254/X/0004/G](#)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Annika Folin

Scope: Grouped application consisting of: 1) extension application to introduce a new strength (184mcg/55mcg/22mcg); 2) extension of indication to add maintenance treatment in adult patients with asthma. As a consequence, sections 2, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 2.2) are updated in accordance

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

5.3.16. [Fluticasone furoate, umeclidinium, vilanterol - TRELEGY ELLIPTA \(CAP\) - EMEA/H/C/004363/X/0012/G](#)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Annika Folin

Scope: Grouped application consisting of: 1) extension application to introduce a new strength (184mcg/55mcg/22mcg); 2) extension of indication to add maintenance treatment in adult patients with asthma. As a consequence, sections 2, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 2.2) are updated in accordance

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

5.3.17. [Guselkumab - TREMFYA \(CAP\) - EMEA/H/C/004271/II/0017](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 5.1) are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.18. [Influenza vaccine surface antigen inactivated prepared in cell cultures - FLUCELVAX TETRA \(CAP\) - EMEA/H/C/004814/II/0013](#)

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to amend the existing indication on prophylaxis of influenza, from the currently approved age range 'adults and children from 9 years of age' to 'adults and children from 2 years of age'. 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 2.1) are updated in accordance

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

5.3.19. [Ipilimumab - YERVOY \(CAP\) - EMEA/H/C/002213/WS1783/0077; nivolumab - OPDIVO \(CAP\) - EMEA/H/C/003985/WS1783/0081](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include first-line treatment of metastatic non-small cell lung cancer (NSCLC) in adults with no epidermal growth factor receptor (EGFR) or anaplastic large-cell lymphoma kinase (ALK) positive tumour mutations for combination of Odivo (nivolumab) and Yervoy (ipilimumab). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. The RMPs (version 17.0 for Opdivo (nivolumab), version 27.0 for Yervoy (ipilimumab)) are updated accordingly

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

5.3.20. [Iron - VELPHORO \(CAP\) - EMEA/H/C/002705/X/0020/G](#)

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped application consisting of: 1) extension application to add a new pharmaceutical form with a new strength - powder for oral suspension 125 mg, 2) extension of indication to add the use of Velporo (iron) for the control of serum phosphorus levels in paediatric patients 2 years of age and older with chronic kidney disease (CKD) stages 4-5 (defined by a glomerular filtration rate (GFR) <30 mL/min/1.73 m²) or with CKD on dialysis, based on the results from study PA-CL-PED-01: an open-label, randomised, active-controlled, parallel group, multicentre, phase 3 study investigating the safety and efficacy of Velporo (iron) and calcium acetate in paediatric and adolescent CKD patients with hyperphosphataemia. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The package leaflet, labelling and the RMP (version 7.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.21. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/X/0083/G, Orphan](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped variations consisting of: 1) extension application to add a new strength of 75 mg film-coated tablets of ivacaftor to enable administration to patients aged 6 to less

than 11 years; 2) update of sections 4.1, 4.2 and 6.5 the SmPC for the 150 mg film-coated tablet presentations to extend the indication for use in children aged 6 to less than 11 years old in combination with tezacaftor/ivacaftor and to bring it in line with the new dosage form. The package leaflet and the RMP (version 8.6) are updated in accordance. In addition, the MAH took the opportunity to implement minor updates throughout the product information

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

5.3.22. [Lurasidone - LATUDA \(CAP\) - EMEA/H/C/002713/II/0029](#)

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

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to add the treatment of schizophrenia in adolescent from 13 to less than 18 years. As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The package leaflet and the RMP (version 8.0) are updated accordingly. In addition, the MAH took the opportunity to update the product information in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' and to update the list of local representatives in the package leaflet

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

5.3.23. [Olaparib - LYNPARZA \(CAP\) - EMEA/H/C/003726/II/0035](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include the use of Lynparza (olaparib) tablets in combination with bevacizumab for the maintenance treatment of adult patients with advanced (FIGO¹¹ stages III and IV) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy with bevacizumab. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC are updated. The package leaflet and the RMP (version 19.0) are updated accordingly. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza (olaparib) hard capsules are revised based on updated safety data analysis. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.24. [Olaparib - LYNPARZA \(CAP\) - EMEA/H/C/003726/II/0036](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include the use of Lynparza (olaparib) tablets as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and homologous recombination repair gene mutations (germline and/or somatic) who have progressed following a prior new hormonal agent. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the

¹¹ International Federation of Gynaecology and Obstetrics

RMP (version 20) are updated accordingly. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza (olaparib) hard capsules are revised based on updated safety data analysis

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

5.3.25. Omalizumab - XOLAIR (CAP) - EMEA/H/C/000606/II/0101

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include treatment of nasal polyps in adult patients with inadequate response to intranasal corticosteroids. 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 16.0) are updated in accordance. In addition, the MAH took the opportunity to introduce minor editorial changes in section 4.2 of the SmPC and in the package leaflet and to update the details of the Dutch local representative. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.26. Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/X/0056

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to introduce a new route of administration (intramuscular use) for the 125 µg solution for injection. The RMP (version 5.1) is updated accordingly

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

5.3.27. Pemetrexed - PEMETREXED ACCORD (CAP) - EMEA/H/C/004072/X/0010

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Adrien Inoubli

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (25 mg/mL solution for infusion). The RMP (version 1.0) is updated accordingly

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

5.3.28. Prucalopride - RESOLOR (CAP) - EMEA/H/C/001012/II/0051

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of Section 4.4 of the SmPC with suicidal ideation and behaviour and to add 'suicidal ideation and behaviour' to the list of safety concerns as an important potential risk in the RMP based on post-marketing reports. The package leaflet and the RMP (version 16.0) are updated accordingly. The MAH took to opportunity to introduce editorial changes to the RMP and SmPC

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

5.3.29. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS1830/0032;
NEPARVIS (CAP) - EMEA/H/C/004343/WS1830/0029

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final report from study CLCZ696D2301 (PARAGON HF) (listed as a category 3 study in the RMP): a multicentre, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of LCZ696 (sacubitril/valsartan) compared to valsartan, on morbidity and mortality in heart failure patients (NYHA¹² class II-IV) with preserved ejection fraction to evaluate cognitive function. The RMP (version 2.0) is updated accordingly

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

5.3.30. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/X/0043/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped applications consisting of: 1) extension application to introduce a new strength (200/50 mg film-coated tablets). The new formulation is indicated for the treatment of chronic hepatitis C (CHC) in patients aged 6 years and older; 2) inclusion of paediatric use in patients aged 6 to <18 years who weigh greater than or equal to 35 kg to the existing presentation (400/100 mg film-coated tablets). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 5.1) are updated in accordance

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

5.3.31. Stiripentol - DIACOMIT (CAP) - EMEA/H/C/000664/X/0032

Applicant: Biocodex

PRAC Rapporteur: Maia Uusküla

Scope: Extension application to add a new strength of 100 mg capsules. The RMP (version 2.0) is updated in accordance

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

5.3.32. Tacrolimus - PROTOPIC (CAP) - EMEA/H/C/000374/II/0083/G

Applicant: LEO Pharma A/S

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC following results from two non-interventional PASS, namely: 1) JOELLE study (listed as a category 3 study in the RMP): a joint European longitudinal lymphoma and skin cancer evaluation; 2) APPLES study (listed as a category 3 study in the RMP): a prospective paediatric longitudinal evaluation to assess the long-term safety of tacrolimus ointment for the treatment of atopic dermatitis. The package leaflet and the RMP (version 15.1) are updated accordingly. In addition, the

¹² New York Heart Association

MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.33. [Tezacaftor, ivacaftor - SYMKEVI \(CAP\) - EMEA/H/C/004682/X/0015/G, Orphan](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped variations consisting of: 1) extension application to add a new strength of 50/75mg film-coated tablets of tezacaftor/ivacaftor to enable administration to patients aged 6 to less than 11 years; 2) update of sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.1 of the SmPC for the 100/150 mg film-coated tablet presentations to extend the indication for use in children aged 6 to less than 11 years old in combination with ivacaftor and to bring it in line with the new dosage form. The package leaflet and the RMP (version 2.1) are updated in accordance. In addition, the MAH took the opportunity to implement minor updates in the product information

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

6. Periodic safety update reports (PSURs)

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

6.1.1. [Aclidinium bromide, formoterol fumarate dihydrate - BRIMICA GENUAIR \(CAP\); DUAKLIR GENUAIR \(CAP\) - PSUSA/00010307/201911](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. [Artenimol, piperazine tetraphosphate - EURARTESIM \(CAP\) - PSUSA/00001069/201910](#)

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. [Atezolizumab - TECENTRIQ \(CAP\) - PSUSA/00010644/201911](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. 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/00010505/201911

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP¹³

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.5. Avatrombopag - DOPTLET (CAP) - PSUSA/00010779/201911

Applicant: Dova Pharmaceuticals Ireland Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Bazedoxifene - CONBRIZA (CAP) - PSUSA/00000302/201910

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Benralizumab - FASENRA (CAP) - PSUSA/00010661/201911

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Buprenorphine¹⁴ - SIXMO (CAP) - PSUSA/00010778/201911

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

¹³ Advanced therapy medicinal product

¹⁴ Implant(s) only

6.1.9. **Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - PSUSA/00010449/201911**

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. **Dalbavancin - XYDALBA (CAP) - PSUSA/00010350/201911**

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. **Daratumumab - DARZALEX (CAP) - PSUSA/00010498/201911**

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

6.1.12. **Dinutuximab beta - QARZIBA (CAP) - PSUSA/00010597/201911**

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. **Dolutegravir, rilpivirine - JULUCA (CAP) - PSUSA/00010689/201911**

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. **Emicizumab - HEMLIBRA (CAP) - PSUSA/00010668/201911**

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Empagliflozin, linagliptin - GLYXAMBI (CAP) - PSUSA/00010539/201911

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Erenumab - AIMOVIG (CAP) - PSUSA/00010699/201911

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Etelcalcetide - PARSABIV (CAP) - PSUSA/00010533/201911

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Fluciclovine (¹⁸F) - AXUMIN (CAP) - PSUSA/00010594/201911

Applicant: Blue Earth Diagnostics Ireland Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Gemtuzumab ozogamicin - MYLOTARG (CAP) - PSUSA/00010688/201911

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

6.1.20. Glibenclamide¹⁵ - AMGLIDIA (CAP) - PSUSA/00010690/201911

Applicant: Ammtek

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁵ Centrally authorised product(s) only

6.1.21. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed)
- CERVARIX (CAP) - PSUSA/00009175/201911

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Hydrocortisone¹⁶ - PLENADREN (CAP) - PSUSA/00009176/201911

Applicant: Shire Services BVBA

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ibrutinib - IMBRUVICA (CAP) - PSUSA/00010301/201911

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Insulin glargine, lixisenatide - SULIQUA (CAP) - PSUSA/00010577/201911

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Ixazomib - NINLARO (CAP) - PSUSA/00010535/201911

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Ketoconazole¹⁷ - KETOCONAZOLE HRA (CAP) - PSUSA/00010316/201911

Applicant: HRA Pharma Rare Diseases

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

¹⁶ Treatment of adrenal insufficiency, modified-release tablets only

¹⁷ Centrally authorised product(s) only

Action: For adoption of recommendation to CHMP

6.1.27. Larotrectinib - VITRAKVI (CAP) - PSUSA/00010799/201911

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Letermovir - PREVYMIS (CAP) - PSUSA/00010660/201911

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Necitumumab - PORTRAZZA (CAP) - PSUSA/00010471/201911

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Osimertinib - TAGRISSO (CAP) - PSUSA/00010472/201911

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Padeliporfin - TOOKAD (CAP) - PSUSA/00010654/201911

Applicant: Steba Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Pegvaliase - PALYNZIQ (CAP) - PSUSA/00010761/201911

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Prasterone¹⁸ - INTRAROSA (CAP) - PSUSA/00010672/201911

Applicant: Endoceutics S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Prucalopride - RESOLOR (CAP) - PSUSA/00002568/201910

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Rituximab - BLITZIMA (CAP); MABTHERA (CAP); RITEMVIA (CAP); RIXATHON (CAP); RIXIMYO (CAP); TRUXIMA (CAP) - PSUSA/00002652/201911

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

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Rotavirus vaccine pentavalent (live, oral) - ROTATEQ (CAP) - PSUSA/00002666/201911

Applicant: MSD Vaccins

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Rurioctocog alfa pegol - ADYNOVI (CAP) - PSUSA/00010663/201911

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Stiripentol - DIACOMIT (CAP) - PSUSA/00002789/201911

Applicant: Biocodex

PRAC Rapporteur: Maia Uusküla

¹⁸ Pessary, vaginal use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Susoctocog alfa - OBIZUR (CAP) - PSUSA/00010458/201911

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Tenofovir alafenamide - VEMLIDY (CAP) - PSUSA/00010575/201911

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/201911

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Vestronidase alfa - MEPSEVII (CAP) - PSUSA/00010709/201911

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Volanesorsen - WAYLIVRA (CAP) - PSUSA/00010762/201911

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/00000425/201911

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. Tadalafil - ADCIRCA (CAP); CIALIS (CAP); TADALAFIL LILLY (CAP); NAP - PSUSA/00002841/201910

Applicants: Eli Lilly Nederland B.V. (Adcirca, Cialis, Tadalafil Lilly), various

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Calcium salts, colecalciferol (NAP) - PSUSA/00010386/201910

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Clevidipine (NAP) - PSUSA/00010288/201911

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Corticorelin (NAP) - PSUSA/00000876/201910

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Fluticasone, salmeterol¹⁹ (NAP) - PSUSA/00001455/201910

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Human coagulation factor VII (NAP) - PSUSA/00001619/201910

Applicant(s): various

PRAC Lead: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Isoflurane (NAP) - PSUSA/00001786/201910

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Isoniazid (NAP) - PSUSA/00001789/201911

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Lenograstim (NAP) - PSUSA/00001839/201910

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Methoxyflurane (NAP) - PSUSA/00010484/201911

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

¹⁹ For nationally approved product(s) only

6.3.10. Ozenoxacin (NAP) - PSUSA/00010651/201911

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. 1-propranolol, 2-propranolol, orthophenylphenol (NAP) - PSUSA/00010406/201910

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Tetrabenazine (NAP) - PSUSA/00002911/201910

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Timolol²⁰ (NAP) - PSUSA/00010432/201910

Applicant(s): various

PRAC Lead: Jana Lukačšínová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Tixocortol (NAP); chlorhexidine gluconate, tixocortol pivalate (NAP) - PSUSA/00010333/201911

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Ceftaroline fosamil - ZINFORO (CAP) - EMEA/H/C/002252/LEG 016

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Maia Uusküla

²⁰ For systemic use only

Scope: Cumulative review on use of ceftaroline in patients with cystic fibrosis and pooled population pharmacokinetic (PK) report based on recently published studies following the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00010013/201810) adopted in May 2019

Action: For adoption of advice to CHMP

6.4.2. Octocog alfa - ADVATE (CAP) - EMEA/H/C/000520/LEG 100

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Review of cases with a fatal outcome and updated information on reports indicative of factor VIII (FVIII) inhibition, following the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00002200/201908) adopted in April 2020

Action: For adoption of advice to CHMP

6.4.3. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/LEG 062.1

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 062 [cumulative review of severe cutaneous skin reactions (SCARs) following the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00002326/201901) adopted in September 2019] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Pirfenidone - ESBRIET (CAP) - EMEA/H/C/002154/II/0066/G, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on drug-induced liver injury (DILI) as requested in the conclusions of LEG 015 concluded in February 2020, assessing a review of cases of serious hepatic reactions and cases of hyponatremia and adequacy of the risk minimisation measures (RMM) of the product information requested in the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00002435/201902) adopted in September 2019. The package leaflet and the RMP (version 10.0) are updated accordingly. In addition, the MAH took the opportunity to amend the package leaflet to reflect information on sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' as well as minor changes; 2) update of sections 4.4 and 4.8 of the SmPC in order to add a warning on hyponatraemia and to add hyponatraemia to the list undesirable effects as requested in the conclusions of LEG 015 assessing a review of cases of hyponatremia requested in the conclusions of PSUSA procedure (PSUSA/00002435/201902)

Action: For adoption of PRAC Assessment Report

6.5.2. Vismodegib - ERIVEDGE (CAP) - EMEA/H/C/002602/II/0046

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Submission of an update of the educational materials as part of the pregnancy prevention programme in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010140/201901) finalised in September 2019. Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 14.0) are updated accordingly. Furthermore, section 4.4 of the SmPC is updated to remove the warning on cutaneous squamous cell carcinoma. Finally, the MAH took the opportunity to update the package leaflet to implement the statement on 'sodium' content in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)²¹

7.1.1. Buprenorphine – SIXMO (CAP) - EMEA/H/C/PSP/S/0086.1

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

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to PSP/S/0086 [protocol for study MOLTeNI-2019-01: a prospective, observational (non-interventional), post-authorisation safety cohort study to evaluate the incidence of the breakages and insertion/removal complications of buprenorphine implants (Sixmo) in the routine clinical care] as per the request for supplementary information (RSI) adopted in February 2020

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

7.1.2. Direct acting antivirals (DAAV):

Dasabuvir - EXVIERA (CAP); elbasvir, grazoprevir – ZEPATIER (CAP); glecaprevir, pibrentasvir – MAVIRET (CAP); ledipasvir, sofosbuvir - HARVONI (CAP); ombitasvir, periteprevir, ritonavir – VIEKIRAX (CAP); sofosbuvir – SOVALDI (CAP); sofosbuvir, velpatasvir – EPCLUSA (CAP); sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/PSA/J/0055

Applicant: Gilead Science International (on behalf of a consortium)

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Substantial amendment for a joint protocol previously agreed in June 2018 (PSA/J/0028.1) for a non-interventional imposed PASS on early recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAAV) therapy in order to estimate the risk of early HCC recurrence associated with DAAV therapy exposure relative to no DAAV therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as required in the outcome of the referral

²¹ In accordance with Article 107n of Directive 2001/83/EC

procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMA/H/A-20/1438)

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

7.1.3. Dinutuximab beta – QARZIBA (CAP) - EMA/H/C/PSA/S/0047.1

Applicant: EUSA Pharma (UK) Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to PSA/S/0047 [substantial amendment to a previously agreed protocol (PSP/S/0065) in July 2018: a registry of patients with high-risk neuroblastoma being treated with Qarziba (dinutuximab beta) to assess: 1) pain severity and use of analgesics during treatment; 2) incidence of neurotoxicity, visual impairment, capillary leak syndrome, cardiovascular events and hypersensitivity reactions; 3) long term safety] as per the request for supplementary information (RSI) adopted in February 2020

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

7.1.4. Eliglustat – CERDELGA (CAP) - EMA/H/C/PSA/S/0054

Applicant: Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Substantial amendment to a protocol previously agreed in December 2018 (PSA/S/0035) for a prospective multicentre observational post authorisation safety sub-registry to characterize the long-term safety profile of commercial use of Cerdelga (eliglustat) in adult patients with Gaucher disease

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

7.1.5. Methylphenidate hydrochloride (NAP) - EMA/H/N/PSP/S/0064.4

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0064.3 [protocol for a multicentre, observational, prospective PASS to evaluate the safety concerns of long-term cardiovascular and psychiatric risks within the adult attention deficit/hyperactivity disorder (ADHD) population taking Medikinet Retard (methylphenidate hydrochloride) according to normal standard clinical practice] as per the request for supplementary information (RSI) adopted in January 2020

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

7.1.6. Parathyroid hormone – NATPAR (CAP) - EMA/H/C/PSA/S/0053

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Substantial amendment to a protocol previously agreed in March 2018 (PSA/S/0026) for study PARADIGHM (physicians advancing disease knowledge in hypoparathyroidism): a registry for subjects with chronic hypoparathyroidism to explore physicians advancing

disease knowledge in hypoparathyroidism

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)²²

7.2.1. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/MEA 053.3

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 053.2 [amendment to a previously agreed protocol for study M07-001: a prospective registry for an observational, multicentre, multinational study of patients with paroxysmal nocturnal haemoglobinuria (PNH)] as per the request for supplementary information (RSI) adopted in February 2020

Action: For adoption of advice to CHMP

7.2.2. Eluxadoline - TRUBERZI (CAP) - EMEA/H/C/004098/MEA 005.4

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 005.3 [amendment to a previously agreed protocol (version 2.0) for study EVM-19596-00-001 (listed as a category 3 study in the RMP): a drug utilisation study (DUS) using relevant healthcare databases at two different time periods in order to define the compliance to contraindications over time and the number of subjects diagnosed with pancreatitis after eluxadoline treatment] as per the request for supplementary information (RSI) adopted in February 2020

Action: For adoption of advice to CHMP

7.2.3. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/MEA 027.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 027 [protocol for study EXCEED (listed as a category 3 study in the RMP): a pan-European PASS to assess the risk of pancreatic cancer among type 2 diabetes mellitus (T2DM) patients who initiated exenatide as compared with those who initiated other non-glucagon-like peptide 1 receptor agonists based glucose lowering drugs] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.2.4. Exenatide - BYETTA (CAP) - EMEA/H/C/000698/MEA 047.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 027 [protocol for study EXCEED (listed as a category 3 study

²² 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

in the RMP): a pan-European PASS to assess the risk of pancreatic cancer among type 2 diabetes mellitus (T2DM) patients who initiated exenatide as compared with those who initiated other non-glucagon-like peptide 1 receptor agonists based glucose lowering drugs] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.2.5. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/MEA 009.1

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: MAH's response to MEA 009 [protocol for study EPI-ZOSTER-030 VS (targeted safety study): a non-interventional/observational prospective cohort study to evaluate the safety of Shingrix (herpes zoster vaccine) in older adults (≥ 50 year of age) in the United States [final clinical study report (CSR) expected in March 2025] (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.2.6. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/MEA 020.1

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: MAH's response to MEA 020 [protocol for study EPI-ZOSTER-032 VS: a non-interventional/observational targeted safety study to evaluate the safety of Shingrix (herpes zoster vaccine) in the Medicare population (65 years old or older) in the United States [final clinical study report (CSR) expected in June 2027]] as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.2.7. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/MEA 002

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Protocol for a study (listed as a category 3 study in the RMP) on pregnancy outcomes intensive monitoring (PRIM) in order to prospectively collect and evaluate safety data on pregnancy outcomes and congenital malformations related to siponimod exposure immediately before and during pregnancy [final clinical study report (CSR) expected in 2030] (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CHMP

7.2.8. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/MEA 004

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Protocol for a survey study (listed as a category 3 study in the RMP) among healthcare professionals (HCPs) and patients/caregivers in selected European countries in order to evaluate whether HCPs and patients/caregivers receive the educational materials and to capture their knowledge and behaviour around specific siponimod safety measures (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CHMP

7.2.9. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/MEA 016

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adrien Inoubli

Scope: Amendment to a protocol previously agreed by CHMP for study B3461001: a sub-analysis of 'transthyretin amyloidosis outcomes survey (THAOS)': a global, multicentre, longitudinal, observational survey of patients with documented transthyretin (TTR) gene mutations or wild-type ATTR amyloidosis, in order to evaluate the effects of tafamidis in non-V30M patients

Action: For adoption of advice to CHMP

7.2.10. Upadacitinib - RINVOO (CAP) - EMEA/H/C/004760/MEA 003

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study P19-150: a long-term post-authorisation safety study (PASS) of upadacitinib use in rheumatoid arthritis (RA) patients in Europe to evaluate the safety of upadacitinib among patients with RA receiving routine clinical care (from initial opinion/marketing authorisation(s) (MA)) [final study report expected in March 2030]

Action: For adoption of advice to CHMP

7.2.11. Upadacitinib - RINVOO (CAP) - EMEA/H/C/004760/MEA 004

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study P19-141: a long-term post-authorisation safety study (PASS) of upadacitinib use in rheumatoid arthritis (RA) patients in the US in order to: 1) compare the incidence of malignancy, non-melanoma skin cancer (NMSC), major adverse cardiovascular events (MACE), venous thromboembolism (VTE) and serious infection events in adults with RA who receive upadacitinib in the course of routine clinical care relative to those who receive biologic therapy for the treatment of RA; 2) describe the incidence rates of herpes zoster, opportunistic infections and evidence of drug-induced liver injury (DILI); 3) describe the incidence of the above outcomes in very elderly patients (aged ≥ 75 years); 4) characterise VTE clinical risk factors and baseline biomarkers in a sub-study of new initiators of upadacitinib and comparator biologic therapies (from initial opinion/marketing authorisation(s) (MA)) [final study report expected in March 2033]

Action: For adoption of advice to CHMP

7.2.12. Upadacitinib - RINVOO (CAP) - EMEA/H/C/004760/MEA 005

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study P20-199: a drug utilisation study (DUS) to evaluate the effectiveness of the additional risk minimisation measures (aRMM) in place to describe the baseline characteristics of new users of upadacitinib, and in a similar manner, to describe new users of a biological disease-modifying antirheumatic drugs (bDMARD) for comparison (from initial opinion/marketing authorisation(s) (MA)) [final study report expected in September 2024]

Action: For adoption of advice to CHMP

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

None

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

7.4.1. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0072/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of the submission of the final reports for : 1) study 20101363 (listed as a category 3 study in the RMP): a non-interventional pharmacovigilance study of osteonecrosis of the jaw and infection leading to hospitalisation among patients with cancer treated with Xgeva (denosumab) or zoledronic acid in Sweden, Denmark and Norway; 2) study 20170728 (listed as a category 3 study in the RMP): a retrospective cohort study on incidence of new primary malignancies among patients with bone metastases from breast, prostate, or lung cancer treated with Xgeva (denosumab) or intravenous zoledronic acid. The RMP (version 35.0) is updated accordingly. In addition, the RMP is brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

7.4.2. Duloxetine - CYMBALTA (CAP) - EMEA/H/C/000572/WS1755/0083; DULOXETINE LILLY (CAP) - EMEA/H/C/004000/WS1755/0020; XERISTAR (CAP) - EMEA/H/C/000573/WS1755/0086; YENTREVE (CAP) EMEA/H/C/000545/WS1755/0068

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study FIJ-MC-B059: an observational study to assess foetal outcomes following maternal exposure to duloxetine and the revised final report from study F1J-MC-B057: an observational study to assess maternal and foetal

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

²⁴ In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

outcomes following exposure to duloxetine

Action: For adoption of PRAC Assessment Report

7.4.3. Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/II/0033

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final study report for study 178-CL-114: an evaluation of cardiovascular events in users of mirabegron and other treatments for overactive bladder

Action: For adoption of PRAC Assessment Report

7.4.4. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0023

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final report from study A3921205 (listed as a category 3 study in the RMP): an observational, PASS within the Consortium of Rheumatology Researchers of North America (CORRONA) registry comparing rates of malignancy, cardiovascular and serious infection outcomes among patients treated for moderately to severely active rheumatoid arthritis. The RMP (version 10.1) is updated accordingly

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. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.14

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of advice to CHMP

7.5.2. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 013.5

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 013.4 [interim report for study BEL114256/ HGS1006-C1101: a pregnancy register collecting information on pregnancy and live birth outcomes, and following infants for serious infections during the first year of life [final report submission extended from April 2019 to April 2022]] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.5.3. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 007.7

Applicant: Hexal AG

PRAC Rapporteur: Menno van der Elst

Scope: 5-year interim results 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, in light of available data [final clinical study report (CSR) expected in December 2024]

Action: For adoption of advice to CHMP

7.5.4. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.7

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: 5-year interim results 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, in light of available data [final clinical study report (CSR) expected in December 2024]

Action: For adoption of advice to CHMP

7.5.5. Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/MEA 041.3

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Fourth interim report for the 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

7.5.6. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/ANX 041.8

Applicant: Celgene Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Second interim descriptive report for study CC-5013-MDS-012 (listed as a category 1 study in Annex II): a post-authorisation, non-interventional, retrospective, drug-utilisation study (DUS) to describe the pattern of use of lenalidomide in patients with myelodysplastic syndromes (MDS)

Action: For adoption of advice to CHMP

7.5.7. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/MEA 036.6

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Adrien Inoubli

Scope: Annual report (covering the period from 01 February 2019 to 31 January 2020) for a drug utilisation study (DUS) on the effectiveness of risk minimisation measures (RMM) for multiple patch use

Action: For adoption of advice to CHMP

7.5.8. Rivastigmine - PROMETAX (CAP) - EMEA/H/C/000255/MEA 037.6

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Adrien Inoubli

Scope: Annual report (covering the period from 01 February 2019 to 31 January 2020) for a drug utilisation study (DUS) on the effectiveness of risk minimisation measures (RMM) for multiple patch use

Action: For adoption of advice to CHMP

7.5.9. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 002.5

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Third 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

7.5.10. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 004.7

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Third interim report 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 report expected in Q2/2020]

Action: For adoption of advice to CHMP

7.5.11. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/MEA 002.2

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Third 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 003.4

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Third interim report 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 report expected in Q2/2020]

Action: For adoption of advice to CHMP

7.5.13. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/MEA 002.4

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: 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 001.5

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Third annual interim report for PASS AC-065A401 (EXPOSURE): an observational cohort study of pulmonary arterial hypertension (PAH) patients newly treated with either Upravi (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. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 018.3

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Fourth 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

7.5.16. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.7

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Second interval safety report 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. Dabrafenib - TAFINLAR (CAP) - EMEA/H/C/002604/MEA 013.3

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Annual report (integrated safety analysis report) for clinical studies: 1) study BRF113683 (BREAK-3): a two-arm, open-label, randomised phase 3 pivotal study comparing oral dabrafenib with intravenous dacarbazine (DTIC), 2) study MEK115306 (COMBI-d): a two-arm, double-blinded, randomised, phase 3 study comparing dabrafenib and trametinib combination therapy with dabrafenib administered with a trametinib placebo (dabrafenib monotherapy); 3) study MEK116513 (COMBI-v): a 2-arm, randomised, open-label, phase 3 study comparing dabrafenib and trametinib combination therapy with vemurafenib monotherapy in BRAF V600 mutation-positive metastatic melanoma on secondary malignancies in patients treated with dabrafenib in randomised controlled trials to comply with the additional pharmacovigilance activity as requested in the RMP; 4) study BRF115531 (COMBI-AD): a 2-arm, randomised, double-blind, phase 3 study of dabrafenib in combination with trametinib versus two matching placebos in the adjuvant treatment of melanoma after surgical resection

Action: For adoption of advice to CHMP

7.6.2. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/LEG 028.1

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adrien Inoubli

Scope: Second six-monthly update on the development of 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

7.6.3. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/MEA 062.2

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to MEA 062 [feasibility report for an international, exploratory, retrospective non-interventional study to collect long-term safety data including malignancies in children with growth failure who have received at least 3 years of Increlex (mecasermin) therapy and followed at least 5 years after the end of Increlex (mecasermin) treatment (from variation II/60 concluded in November 2019)] as per the request for supplementary information (RSI) adopted in March 2020

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. [Amifampridine - FIRDAPSE \(CAP\) - EMEA/H/C/001032/S/0066 \(without RMP\)](#)

Applicant: SERB SA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. [Clofarabine - EVOLTRA \(CAP\) - EMEA/H/C/000613/S/0068 \(without RMP\)](#)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. [Susoctocog alfa - OBIZUR \(CAP\) - EMEA/H/C/002792/S/0028 \(without RMP\)](#)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/003922/S/0011 (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. Larotrectinib - VITRAKVI (CAP) - EMEA/H/C/004919/R/0006 (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. Asparaginase - SPECTRILA (CAP) - EMEA/H/C/002661/R/0018 (without RMP)

Applicant: Medac Gesellschaft für klinische Spezialpräparate mbH

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Cholic acid - KOLBAM (CAP) - EMEA/H/C/002081/R/0034 (with RMP)

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Agni Kapou

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Duloxetine - DULOXETINE ZENTIVA (CAP) - EMEA/H/C/003935/R/0009 (with RMP)

Applicant: Zentiva k.s.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Efmoroctocog alfa - ELOCTA (CAP) - EMEA/H/C/003964/R/0036 (with RMP)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Sonja Hrabcik

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/R/0053 (without RMP)

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Glycerol phenylbutyrate - RAVICTI (CAP) - EMEA/H/C/003822/R/0034 (without RMP)

Applicant: Immedica Pharma AB

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Pemetrexed - ARMISARTE (CAP) - EMEA/H/C/004109/R/0022 (with RMP)

Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Pemetrexed - PEMETREXED HOSPIRA (CAP) - EMEA/H/C/003970/R/0022 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Pemetrexed - PEMETREXED MEDAC (CAP) - EMEA/H/C/003905/R/0008 (with RMP)

Applicant: medac Gesellschaft für klinische Spezialpräparate mbH

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Pemetrexed - PEMETREXED SANDOZ (CAP) - EMEA/H/C/004011/R/0008 (without RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. Pandemic - monthly summary safety reports - process for submission and assessment

Action: For discussion

12.1.2. Pandemic - monthly summary safety reports – assessment report template

Action: For adoption

12.2. Coordination with EMA Scientific Committees or CMDh-v

12.2.1. Committee for Medicinal Products for Human Use (CHMP)-PRAC collaboration group –proposals for improvements

PRAC lead: Martin Huber, Adrien Inoubli, Ulla Wändel Liminga

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

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.15.3. COVID-19-vaccine monitoring – ACCESS²⁵ project - preparation

PRAC lead: Jean Michel Dogne, Brigitte Keller-Stanislawski, Adrien Inoubli

Action: For discussion

12.15.4. Registry-based studies –guideline - draft

PRAC lead: Virginie Hivert, Brigitte Keller-Stanislawski, Sabine Straus, Ulla Wändel Liminga

Action: For discussion

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Drug-induced hepatotoxicity - PRAC assessors' guide - draft

PRAC lead: Menno van der Elst, Martin Huber

Action: For adoption

12.20.2. Serious cutaneous adverse reactions (SCARs) - PRAC assessors' guide - update

PRAC lead: Sabine Straus, Zane Neikena

Action: For adoption

²⁵ vACCine Covid-19 monitoring readinESS

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=WCOB01ac05800240d0

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/