EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 October 2020
EMA/PRAC/570668/2020
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 26-29 October 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

26 October 2020, 10:30 – 19:30, via teleconference

27 October 2020, 08:30 – 19:30, via teleconference

28 October 2020, 08:30 – 19:30, via teleconference

29 October 2020, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

12 November 2020, 09:00 – 12:00, via teleconference

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 26-29 October 2020. See November 2020 PRAC minutes (to be published post December 2020 PRAC meeting).

1.2. Agenda of the meeting on 26-29 October 2020

Action: For adoption

1.3. Minutes of the previous meeting on 28 September-01 October 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. Ifosfamide[1] (NAP) - EMEA/H/A-31/1495

Applicant(s): various

PRAC Rapporteur: Martin Huber; PRAC Co-rapporteur: Nikica Mirošević Skvrce

[1] Solution, concentrate for solution

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

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

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Immune checkpoint inhibitors: atezolizumab – TECENTRIQ (CAP); avelumab – BAVENCIO (CAP); cemiplimab – LIBTAYO (CAP); durvalumab – IMFINZI (CAP); ipilimumab – YERVOY (CAP); pembrolizumab – KEYTRUDA (CAP); nivolumab - OPDIVO (CAP)

Applicant(s): AstraZeneca AB (Imfinzi), Bristol-Myers Squibb Pharma (Opdivo, Yervoy), Merck Europe B.V. (Bavencio), Merck Sharp & Dohme B.V. (Keytruda), Regeneron Ireland Designated (Libtayo), Roche Registration GmbH (Tecentriq)

PRAC Rapporteur: To be appointed

Scope: Signal of immune-mediated cystitis

Action: For adoption of PRAC recommendation

EPITT 19610 – New signal

Lead Member State(s): DE, DK, NL, NO, PT

4.2. New signals detected from other sources

4.2.1. Cannabidiol – EPIDYOLEX (CAP); tacrolimus[4] - ADVAGRAF (CAP), ENVARSUS (CAP), MODIGRAF (CAP), TACFORIUS (CAP); NAP

Applicant(s): Astellas Pharma Europe B.V. (Advagraf, Modigraf), Chiesi Farmaceutici S.p.A. (Envarsus), GW Pharma (International) B.V. (Epidyolex), Teva B.V. (Tacforius), various

PRAC Rapporteur: To be appointed

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

Scope: Signal of drug interaction with cannabidiol leading to tacrolimus serum level increased and toxicity

Action: For adoption of PRAC recommendation

EPITT 19614 – New signal

Lead Member State(s): IE, PT, SE

4.2.2. Trastuzumab emtansine – KADCYLA (CAP)

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of extravasation and epidermal necrosis

Action: For adoption of PRAC recommendation

EPITT 19611 – New signal

Lead Member State(s): DK

4.3. Signals follow-up and prioritisation

4.3.1. Anakinra - KINERET (CAP) - EMEA/H/C/000363/SDA/032; canakinumab - ILARIS (CAP) - EMEA/H/C/001109/SDA/054

Applicant(s): Novartis Europharm Limited (Ilaris), Swedish Orphan Biovitrum AB (publ) (Kineret)

PRAC Rapporteur: Hans Christian Siersted

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

Action: For adoption of PRAC recommendation

EPITT 19566 – Follow-up to July 2020

4.3.2. Cefepime (NAP)

Applicant(s): various

PRAC Rapporteur: Ana Sofia Diniz Martins

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

Action: For adoption of PRAC recommendation

EPITT 17866 – Follow-up to June 2020

4.3.3. Ceftriaxone (NAP)

Applicant(s): various

PRAC Rapporteur: Zane Neikena

Scope: Signal of encephalopathy

Action: For adoption of PRAC recommendation

EPITT 19492 – Follow-up to April 2020

4.3.4. Dabrafenib - TAFINLAR (CAP) - EMEA/H/C/002604/SDA/018; trametinib - MEKINIST (CAP) - EMEA/H/C/002643/SDA/013

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: David Olsen

Scope: Signal of sarcoidosis

Action: For adoption of PRAC recommendation

EPITT 19574 – Follow-up to July 2020

4.3.5. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/SDA/031

Applicant(s): Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Signal of hepatitis E

Action: For adoption of PRAC recommendation

EPITT 19569 – Follow-up to July 2020

4.3.6. Immune checkpoint inhibitors: atezolizumab – TECENTRIQ (CAP) – EMEA/H/C/004143/SDA/020; avelumab – BAVENCIO (CAP) – EMEA/H/C/004338/SDA/006; cemiplimab – LIBTAYO (CAP) - EMEA/H/C/004844/SDA/006; durvalumab – IMFINZI (CAP) - EMEA/H/C/004771/SDA/006; ipilimumab – YERVOY (CAP) – EMEA/H/C/002213/SDA/040; pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/026; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/SDA/041

Applicant(s): AstraZeneca AB (Imfinzi), Bristol-Myers Squibb Pharma (Opdivo, Yervoy), Merck Europe B.V. (Bavencio), Merck Sharp & Dohme B.V. (Keytruda), Regeneron Ireland Designated (Libtayo), Roche Registration GmbH (Tecentriq)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of eosinophilic fasciitis

Action: For adoption of PRAC recommendation

EPITT 19567 – Follow-up to June 2020

4.3.7. Lamotrigine (NAP)

Applicant(s): various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of photosensitivity

Action: For adoption of PRAC recommendation

EPITT 19548 – Follow-up to March 2020

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0019

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on diverticulitis following the recommendation of signal procedure SDA/010 (EPITT 19496) adopted in May 2020. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Adalimumab - EMEA/H/C/005188

Scope: Treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, juvenile idiopathic arthritis, enthesitis-related arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis and paediatric uveitis

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

5.1.2. Bevacizumab - EMEA/H/C/005640

Scope: Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and metastatic or recurrent non-small cell lung cancer, advanced and/or metastatic renal cell cancer, epithelial ovarian, fallopian tube, or primary peritoneal cancer and persistent, recurrent, or metastatic carcinoma of the cervix. First-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer. First line treatment of patients with advanced and/or metastatic renal cell cancer

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

5.1.3. Estetrol, drospirenone - EMEA/H/C/005336

Scope: Oral contraception

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

5.1.4. Estetrol, drospirenone - EMEA/H/C/005382

Scope: Oral contraception

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

5.1.5. Lisocabtagene maraleucel - EMEA/H/C/004731, Orphan

Applicant: Celgene Europe BV, ATMP[5]

Scope (accelerated assessment): Treatment of large B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B)

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

5.1.6. Risdiplam - EMEA/H/C/005145, Orphan

Applicant: Roche Registration GmbH

Scope (accelerated assessment): Treatment of spinal muscular atrophy (SMA)

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. Agomelatine - THYMANAX (CAP) - EMEA/H/C/000916/WS1849/0045; VALDOXAN (CAP) - EMEA/H/C/000915/WS1849/0047

Applicant(s): Les Laboratoires Servier (Valdoxan), Servier (Ireland) Industries Ltd. (Thymanax)

PRAC Rapporteur: Pernille Harg

Scope: Submission of an updated RMP (version 23.1) in order to revise the list of safety concerns, important identified and potential risks in line with revision 2 of GVP module V on 'Risk management systems'. In addition, the completed studies have been deleted and, as agreed in the conclusions of LEG 031 adopted in January 2019, the frequency of the educational material distribution is updated to once yearly

Action: For adoption of PRAC Assessment Report

5.2.2. Histamine dihydrochloride - CEPLENE (CAP) - EMEA/H/C/000796/II/0040

Applicant: Noventia Pharma S.r.l.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP (version 8.1) in order to include information about the termination/finalisation of: 1) non-interventional study Ceplene-3290 (listed as a category 3 study in the RMP): an open study designed to gain further knowledge on Ceplene (histamine dihydrochloride) under day to day conditions with special emphasis on tolerability, practicability, usage, and measurable minimal residual disease and course of blast cells and; 2) post-authorisation efficacy study (PAES) Ceplene cohort study 3306: an international, multicentre, observational, non-interventional, registry-based cohort study aiming to describe and evaluate minimal residual disease (MRD) at baseline and follow-up for the assessment of the anti-leukaemic activity of Ceplene (histamine dihydrochloride)/interleukin-2 (IL-2) as remission maintenance therapy in adult patients with acute myeloid leukaemia (AML) in first complete remission (CR1) compared to matched control patients who did not receive Ceplene

[5] Advanced therapy medicinal product

(histamine dihydrochloride)/IL-2. 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). As a consequence, the list of safety concerns is amended in particular 'drug effect decreased as a consequence of drug interaction' is added as a new important potential risk

Action: For adoption of PRAC Assessment Report

5.2.3. Iloprost - VENTAVIS (CAP) - EMEA/H/C/000474/II/0066

Applicant: Bayer AG

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of an updated RMP (version 8.0) to introduce respiratory tract infection as an important potential risk as requested in the conclusions of the periodic safety update report single assessment (PSUSA) procedure (PSUSA/00001724/201709) adopted in May 2018. In addition the MAH took the opportunity to update the RMP in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.4. Mannitol - BRONCHITOL (CAP) - EMEA/H/C/001252/II/0042, Orphan

Applicant: Pharmaxis Europe Limited

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of an updated RMP (version 9.0) brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). The MAH took the opportunity to review the safety information and proposed to reclassify 'cough' from an important potential risk to an important identified risk; to remove the important identified risks of 'bronchospasm during and after the initiation dose assessment' and 'bronchospasm during long term use'; to remove the important potential risk of 'cough-related sequelae', 'off label use in non-cystic fibrosis (CF) bronchiectasis', 'off label use in paediatric/adolescent CF patients (aged 6-17 years)', 'administration of Bronchitol via the wrong inhaler device' and 'starting Bronchitol treatment without completing the full Bronchitol initiation dose assessment (BIDA) dose'; to remove the missing information of 'patients requiring home oxygen or needing assisted ventilation', 'children <6 years of age', 'pregnancy and lactation', 'risks associated with long-term use' from the list of safety concerns; to add 'increased risk of respiratory or systemic infection' as an important potential risk replacing 'pulmonary abscess on continued use', 'septicaemia on continued use', 'increased risk of bacteria sputum identified or infections with extended use of Bronchitol' and 'microbial infection via a contaminated inhaler device' previously classified as important potential risks. In addition, the pharmacovigilance plan is updated with completed studies. Finally, the RMP is updated as requested in the conclusions of the periodic safety update report single assessment (PSUSA) procedure (PSUSA/00009226/201904) adopted at the November 2019 PRAC meeting

Action: For adoption of PRAC Assessment Report

5.2.5. Pramipexole - MIRAPEXIN (CAP) - EMEA/H/C/000134/WS1897/0096; SIFROL (CAP) - EMEA/H/C/000133/WS1897/0087

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 12.0) as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002491/201904) adopted in December 2019 in order to remove cardiac failure from the list of important identified risks and to amend the information on dopamine agonist withdrawal syndrome (DAWS) as an important identified risk

Action: For adoption of PRAC Assessment Report

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

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

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

Action: For adoption of PRAC Assessment Report

5.2.7. 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

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

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Hans Christian Siersted

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

Action: For adoption of PRAC Assessment Report

5.2.9. Umeclidinium bromide - INCRUSE ELLIPTA (CAP) - EMEA/H/C/002809/WS1589/0029; ROLUFTA ELLIPTA (CAP) - EMEA/H/C/004654/WS1589/0014

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

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of an updated RMP (version 7.1) following completion of study WWE117397 (listed as a category 3 in the RMP): a post-authorisation safety electronic medical records database retrospective cohort study of new users of inhaled umeclidinium/vilanterol (UMEC/VI) or new users of inhaled umeclidinium (UMEC) in the primary care setting. In addition, updates are reflected in the RMP with regard to study 201038 (listed as a category 1 in the RMP/Annex II): a post authorisation safety observational cohort study to quantify the incidence of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients using inhaled UMEC/VI combination or inhaled UMEC versus tiotropium, as requested in the conclusions of procedure PSA/S/0032.3 adopted in November 2019. These include updates of the primary and secondary objectives to include the composite endpoint and the sample size for the study. Finally, the RMP is brought in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

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

5.3.1. Avatrombopag - DOPTELET (CAP) - EMEA/H/C/004722/II/0004/G

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) extension of indication to include the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, section 5.3 of the SmPC is updated with data from juvenile toxicity studies; 2) addition of a pack size with subsequent updates of sections 6.5 and 8 of the SmPC. The package leaflet, labelling and the RMP (version 2.1) are updated in accordance. 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

5.3.2. Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - TRIMBOW (CAP) - EMEA/H/C/004257/X/0008/G

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Grouped application consisting of: 1) extension application to introduce a new strength; 2) update of sections 4.1, 4.2, 4.4, 5.1 and 5.2 of the SmPC to extend the indication to the maintenance treatment in adult patients with asthma who are not adequately treated by a combination of an inhaled corticosteroid and a long-acting beta2-agonist or who are already treated by a combination of an inhaled corticosteroid and a long-acting beta2-agonist plus a

long-acting muscarinic antagonist. The RMP (version 6.1) is updated in accordance

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

5.3.3. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0070

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the use of belatacept in conversion from a calcinerin inhibitor-based regimen to a belatacept-based regimen post transplantation. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 18.0) are updated in accordance. Furthermore, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1) and to update it with regard to 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'

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

5.3.4. Carfilzomib - KYPROLIS (CAP) - EMEA/H/C/003790/II/0045, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of existing indication to include combination of Kyprolis (carfilzomib) with daratumumab and dexamethasone. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance

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

5.3.5. 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; 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

5.3.6. 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; 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

5.3.7. 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; 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

5.3.8. Follitropin delta - REKOVELLE (CAP) - EMEA/H/C/003994/II/0022

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.2 of the SmPC in order to introduce a new anti-Müllerian hormone (AMH) assay to determine the dose of follitropin delta, following an agreed recommendation. The RMP (version 5.0) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems'. The MAH took the opportunity to amend section 4.4 of the SmPC to introduce traceability information. Finally, 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

5.3.9. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS1840/0084; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS1840/0089

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) metastatic colorectal cancer (CRC) for combination treatment with Opdivo (nivolumab) and Yervoy (ipilimumab). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMPs (Opdivo version 18.0, Yervoy version 29.0) are updated in accordance

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

5.3.10. Lacosamide - LACOSAMIDE ACCORD (CAP) - EMEA/H/C/004443/X/0007

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to introduce a new pharmaceutical form (solution for infusion), a new strength and a new route of administration (intravenous use). The RMP (version 1.0) is updated accordingly

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

5.3.11. Lipegfilgrastim - LONQUEX (CAP) - EMEA/H/C/002556/II/0058/G

Applicant: Teva B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of an extension of indication to include treatment of the paediatric population and introduction of an age appropriate presentation in vials. 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 12.0) 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

5.3.12. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/X/0116

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength and a new route of administration. The RMP (version 26.1) is updated accordingly

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

5.3.13. Nintedanib - VARGATEF (CAP) - EMEA/H/C/002569/II/0035/G

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Agni Kapou

Scope: Grouped variations consisting of: 1) update of sections 4.5, 4.6 and 5.2 of the SmPC to reflect the results of study 1199-0340 conducted in female patients with systemic sclerosis associated interstitial lung disease (SSc-ILD) to investigate a potential interaction between nintedanib and a combined oral contraceptive (COC) containing ethynilestradiol/levonorgestrel; 2) update of sections 4.3 and 4.6 of the SmPC to introduce a new contraindication of pregnancy. This follows the update for Ofev (nintedanib) on SSc-ILD introduced in the context of variation II/0026 finalised in February 2020 and as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010318/201910) adopted in May 2020. The package leaflet and the RMP (version 7.0) are updated accordingly

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

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.4 in order to include the term ‘anaphylaxis’ among the possible symptoms of infusion-related reactions (IRRs), following an analysis of cases retrieved by

anaphylactic reaction MedDRA[6] narrow standardised MedDRA queries (SMQ). The MAH took the opportunity to update Annex II-C on 'Other conditions and requirements of the marketing authorisation' and Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' 'in line with the latest quality review of documents (QRD) template (version 10.1). The RMP (version 6.0) is updated accordingly

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

5.3.15. Pegvisomant - SOMAVERT (CAP) - EMEA/H/C/000409/II/0098/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adrien Inoubli

Scope: Grouped variations consisting of: 1) update of section 4.4 of the SmPC to remove the warning on growth hormone secreting tumours, consequential to the removal of pituitary tumour growth as a potential risk from the RMP. The package leaflet is updated accordingly; 2) update of the RMP (version 2.0) to reflect the evaluation of the final results of study A6291010 (ACROSTUDY) (listed as a category 3 study in the RMP): an open-label, global, multicentre, non-interventional PASS performed to monitor the long-term safety and outcomes of pegvisomant treatment in clinical practice as per the conclusions of variation II/0089 adopted in July 2019. The RMP is also brought in line with revision 2 of GVP module V on 'Risk management systems'

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

5.3.16. Rituximab - BLITZIMA (CAP) - EMEA/H/C/004723/WS1893/0034; RITEMVIA (CAP) - EMEA/H/C/004725/WS1893/0034; TRUXIMA (CAP) - EMEA/H/C/004112/WS1893/0037

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of the final clinical study report (CSR) for study CT-P10 3.4: a phase 3, randomised, parallel-group, active-controlled, double-blind study to compare efficacy and safety between CT-P10 (Blitzima/Ritemvia/Truxima (biosimilar rituximab)) and Rituxan/Mabthera (rituximab) in patients with low tumour burden follicular lymphoma (LTBFL). The RMP (version 10.1) is updated accordingly

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

5.3.17. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/X/0074/G

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped applications consisting of: 1) extension application to introduce a new pharmaceutical form, granules for oral suspension; 2) extension of indication to include treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in term neonates, infants and toddlers, children and adolescents aged less than 18 years following initiation of standard anticoagulation treatment for Xarelto (rivaroxaban) 15 mg and 20 mg tablets. As a consequence, sections 4.2, 4.4, 4.5, 4.8, 4.9, 5.1 and 5.2 of the SmPC are

[6] Medical Dictionary for Regulatory Activities

updated. The package leaflet and the RMP (version 12.1) are updated accordingly. In addition, sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated for all other dose strengths (2.5/10 mg and 15/20 mg initiation packs). Furthermore, the MAH took the opportunity to update the product information with regards to 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'

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

5.3.18. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/II/0020

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to update the information on the use of rucaparib in patients with hepatic impairment based on final results from part I of study CO-338-078 (listed as a category 3 study in the RMP): a phase 1, open-label, parallel group study to determine the pharmacokinetics, safety and tolerability of rucaparib in patients with an advanced solid tumour and either moderate hepatic impairment or normal hepatic function. The package leaflet and the RMP (version 4.0) are updated accordingly. The MAH took the opportunity to introduce minor corrections in the SmPC, to update the list of local representatives in the package leaflet, and to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1).and in line 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 RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.19. 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 (NYHA[7] 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

5.3.20. Sodium phenylbutyrate - PHEBURANE (CAP) - EMEA/H/C/002500/X/0026

Applicant: Eurocept International B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension application to introduce a new pharmaceutical form associated with a new strenght. The RMP (version 0.1) is updated in accordance

[7] New York Heart Association

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

5.3.21. Sodium phenylbutyrate - PHEBURANE (CAP) - EMEA/H/C/002500/X/0028

Applicant: Eurocept International B.V.

PRAC Rapporteur: Rhea Fitzgerald

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

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

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

Applicant: Biocodex

PRAC Rapporteur: Maia Uusküla

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

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. Abemaciclib - VERZENIOS (CAP) - PSUSA/00010724/202003

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alogliptin - VIPIDIA (CAP); alogliptin, metformin - VIPDOMET (CAP); alogliptin, pioglitazone - INCRESYNC (CAP) - PSUSA/00010061/202004

Applicant(s): Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Avelumab - BAVENCIO (CAP) - PSUSA/00010635/202003

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Brolucizumab - BEOVU (CAP) - PSUSA/00010829/202004

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Canagliflozin - INVOKANA (CAP); canagliflozin, metformin - VOKANAMET (CAP) - PSUSA/00010077/202003

Applicant(s): Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Cemiplimab - LIBTAYO (CAP) - PSUSA/00010780/202003

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Certolizumab - CIMZIA (CAP) - PSUSA/00000624/202003

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Dacomitinib - VIZIMPRO (CAP) - PSUSA/00010757/202003

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Dapagliflozin - EDISTRIDE (CAP); FORXIGA (CAP) - PSUSA/00010029/202004

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Darvadstrocel - ALOFISEL (CAP) - PSUSA/00010676/202003

Applicant: Takeda Pharma A/S, ATMP[8]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.11. Dupilumab - DUPIXENT (CAP) - PSUSA/00010645/202003

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Emtricitabine - EMTRIVA (CAP) - PSUSA/00001209/202004

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Emtricitabine, tenofovir alafenamide - DESCOVY (CAP) - PSUSA/00010515/202004

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - PSUSA/00001210/202004

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Exenatide - BYDUREON (CAP); BYETTA (CAP) - PSUSA/00009147/202003

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

[8] Advanced therapy medicinal product

Action: For adoption of recommendation to CHMP

6.1.16. Fostamatinib - TAVLESSE (CAP) - PSUSA/00010819/202004

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Galcanezumab - EMGALITY (CAP) - PSUSA/00010733/202003

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Gilteritinib - XOSPATA (CAP) - PSUSA/00010832/202003

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - PSUSA/00010678/202004

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Histamine[9] - CEPLENE (CAP) - PSUSA/00001610/202004

Applicant: Noventia Pharma S.r.l.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Insulin glulisine - APIDRA (CAP) - PSUSA/00001752/202004

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Hans Christian Siersted

[9] Indicated for the treatment of acute myeloid leukaemia (AML)

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Ipilimumab - YERVOY (CAP) - PSUSA/00009200/202003

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ixekizumab - TALTZ (CAP) - PSUSA/00010493/202003

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Lorlatinib - LORVIQUA (CAP) - PSUSA/00010760/202003

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Lusutrombopag - MULPLEO (CAP) - PSUSA/00010755/202003

Applicant: Shionogi B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Meningococcal group A, C, W-135, Y conjugate vaccine (conjugated to *Corynebacterium diphtheriae* CRM_{197} protein) - MENVEO (CAP) - PSUSA/00001969/202003

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Mogamulizumab - POTELIGEO (CAP) - PSUSA/00010741/202003

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Naldemedine - RIZMOIC (CAP) - PSUSA/00010753/202003

Applicant: Shionogi B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Nintedanib[10] - OFEV (CAP) - PSUSA/00010319/202004

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Niraparib - ZEJULA (CAP) - PSUSA/00010655/202003

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Ocrelizumab - OCREVUS (CAP) - PSUSA/00010662/202003

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Risankizumab - SKYRIZI (CAP) - PSUSA/00010765/202003

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Siponimod - MAYZENT (CAP) - PSUSA/00010818/202003 (with RMP)

Applicant: Novartis Europharm Limited

[10] Respiratory indication(s) only

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Sodium zirconium cyclosilicate - LOKELMA (CAP) - PSUSA/00010675/202003

Applicant: AstraZeneca AB

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Talazoparib - TALZENNA (CAP) - PSUSA/00010781/202004

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

6.1.36. Trifluridine, tipiracil - LONSURF (CAP) - PSUSA/00010517/202003

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Vandetanib - CAPRELSA (CAP) - PSUSA/00009327/202004

Applicant: Genzyme Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Velmanase alfa - LAMZEDE (CAP) - PSUSA/00010677/202003

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Yttrium (^{90}Y) chloride - YTRACIS (CAP); YTTRIGA (CAP) - PSUSA/00003137/202003

Applicant(s): Cis Bio International (Ytracis), Eckert & Ziegler Radiopharma GmbH (Yttriga)

PRAC Rapporteur: Menno van der Elst

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. Enoxaparin - INHIXA (CAP); NAP - PSUSA/00010833/202004

Applicant(s): Techdow Pharma Netherlands B.V. (Inhixa), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Tenofovir disoproxil - TENOFOVIR DISOPROXIL MYLAN (CAP); TENOFOVIR DISOPROXIL ZENTIVA (CAP); VIREAD (CAP); NAP - PSUSA/00002892/202003

Applicant(s): Gilead Sciences Ireland UC (Viread), Mylan S.A.S (Tenofovir disoproxil Mylan), Zentiva k.s. (Tenofovir disoproxil Zentiva), various

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Zonisamide - ZONEGRAN (CAP); NAP - PSUSA/00003152/202003

Applicant(s): Eisai GmbH, various

PRAC Rapporteur: Ronan Grimes

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. Ascorbic acid, paracetamol, pheniramine maleate (NAP) - PSUSA/00002368/202003

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Ethosuximide (NAP) - PSUSA/00001316/202003

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Fluconazole (NAP) - PSUSA/00001404/202003

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Flucloxacillin (NAP) - PSUSA/00001402/202003

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Galantamine (NAP) - PSUSA/00001512/202003

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Hydroxyethyl starch (HES) (NAP) - PSUSA/00001694/202003

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.3.7. Lanthanum (NAP) - PSUSA/00003175/202003

Applicant(s): various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Metamizole (NAP) - PSUSA/00001997/202003

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Trandolapril, verapamil (NAP) - PSUSA/00003005/202003

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/LEG 050

Applicant: Celgene Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: Detailed review of cases of B-cell acute lymphoblastic leukaemia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001838/201912) adopted in July 2020

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0022, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Update of section 4.8 to add acute febrile neutrophilic dermatosis (Sweet's syndrome), Stevens-Johnson syndrome, transverse myelitis, posterior reversible encephalopathy syndrome, tumour lysis syndrome as requested in the conclusions of the latest periodic safety update report single assessment (PSUSA) procedure (PSUSA/00010535/201911) adopted in June 2020. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[11]

6.6.1. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/MEA 017.3

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Sixth expedited monthly summary safety report for remdesivir for October 2020 including spontaneously reported data and data from compassionate use and expanded access programmes for the duration of the coronavirus disease (COVID-19) pandemic

[11] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[12]

7.1.1. Betibeglogene autotemcel – ZYNTEGLO (CAP) - EMEA/H/C/PSA/S/0059

Applicant: Bluebird bio (Netherlands) B.V., ATMP[13]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for a non-interventional PASS to collect longitudinal data on clinical outcomes of patients with transfusion-dependent β-thalassaemia (TDT) who have received treatment with Zynteglo (betibeglogene autotemcel) in the post-marketing setting

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

7.1.2. Eliglustat – CERDELGA (CAP) - EMEA/H/C/PSA/S/0054.1

Applicant: Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to PSA/S/0054 [substantial amendment to a protocol previously agreed in December 2018 (PSA/S/0035) for a prospective multicentre observational post authorisation safety sub-registry to characterise the long-term safety profile of commercial use of Cerdelga (eliglustat) in adult patients with Gaucher disease] as per the request for supplementary information (RSI) adopted in June 2020

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

7.1.3. Methylphenidate hydrochloride (NAP) - EMEA/H/N/PSP/S/0064.5

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG (Medikinet)

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0064.4 [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 June 2020

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

7.1.4. Parathyroid hormone – NATPAR (CAP) - EMEA/H/C/PSA/S/0053.1

Applicant: Shire Pharmaceuticals Ireland

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to PSA/S/0053 [substantial amendment to a protocol previously agreed in March 2018 (PSA/S/0026) for study PARADIGHM (physicians advancing disease

[12] In accordance with Article 107n of Directive 2001/83/EC
[13] Advanced therapy medicinal product

knowledge in hypoparathyroidism): a registry for subjects with chronic hypoparathyroidism to explore physicians advancing disease knowledge in hypoparathyroidism] as per the request for supplementary information (RSI) adopted in June 2020

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[14]

7.2.1. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/MEA 092.1

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 092 [protocol for study 20190404: a retrospective cohort study to assess the use of erythropoiesis stimulating agents (ESAs) in subjects receiving myelosuppressive chemotherapy in Europe] as per the request for supplementary information (RSI) adopted in May 2020

Action: For adoption of advice to CHMP

7.2.2. Interferon beta-1a - AVONEX (CAP) - EMEA/H/C/000102/MEA 088.1

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 088 [protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden] as per the request for supplementary information (RSI) adopted in April 2020

Action: For adoption of advice to CHMP

7.2.3. Interferon beta-1a - REBIF (CAP) - EMEA/H/C/000136/MEA 045.1

Applicant: Merck Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 045 [protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden] as per the request for supplementary information (RSI) adopted in April 2020

Action: For adoption of advice to CHMP

7.2.4. Interferon beta-1b - BETAFERON (CAP) - EMEA/H/C/000081/MEA 025.1

Applicant: Bayer AG

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 025 [protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of

[14] 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

pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden] as per the request for supplementary information (RSI) adopted in April 2020

Action: For adoption of advice to CHMP

7.2.5. Interferon beta-1b - EXTAVIA (CAP) - EMEA/H/C/000933/MEA 023.1

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 023 [protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden] as per the request for supplementary information (RSI) adopted in April 2020

Action: For adoption of advice to CHMP

7.2.6. Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/MEA 004

Applicant: Celgene Europe BV

PRAC Rapporteur: Laurence de Fays

Scope: Amendment to a protocol previously agreed in the framework of the initial marketing authorisation application (MAA) procedure for study ACE-536-LTFU-001: a phase 3b, open label, single-arm rollover study to evaluate long term safety in subjects who have participated in other luspatercept clinical trials in order to amend the iron parameters

Action: For adoption of advice to CHMP

7.2.7. Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/MEA 010.1

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 010 [protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden] as per the request for supplementary information (RSI) adopted in April 2020

Action: For adoption of advice to CHMP

7.2.8. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/MEA 002.1

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Substantial amendment to a protocol previously agreed in September 2018 (MEA 002) for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in patients with type 2 diabetes mellitus (T2DM) taking semaglutide - a cohort study based on Nordic registry data [final study report expected 5 years after start of study]

Action: For adoption of advice to CHMP

7.2.9. Semaglutide - RYBELSUS (CAP) - EMEA/H/C/004953/MEA 002

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Substantial amendment to a protocol previously agreed in September 2018 (Ozempic MEA 002) for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in patients with type 2 diabetes mellitus (T2DM) taking semaglutide - a cohort study based on Nordic registry data [final study report expected 5 years after start of study]

Action: For adoption of advice to CHMP

7.2.10. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 015.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 015 [protocol for study A3921334: a non-interventional PASS to evaluate the effectiveness of additional risk minimisation measures (aRMM) materials for Xeljanz (tofacitinib) in Europe via a survey of healthcare professionals (HCPs), as requested in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1485) finalised in November 2019] as per the request for supplementary information (RSI) adopted in July 2020

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[15]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[16]

7.4.1. Aclidinium - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/WS1795/0043; EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/WS1795/0043

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from study D6570R00002 (listed as a category 3 study in the RMP): a descriptive, non-interventional, multinational European cohort study of new users of aclidinium, aclidinium/formoterol, and other selected chronic obstructive pulmonary disease (COPD) medications to describe the characteristics and patterns of use. As a consequence, the following safety concerns listed as missing information in the RMP are removed: 'safety in patients with hepatic or severe renal impairment', 'safety in patients with benign hyperplasia or urinary retention' and 'use in pregnancy or lactation'. The RMP (version 8.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

[15] In accordance with Article 107p-q of Directive 2001/83/EC
[16] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

7.4.2. Aclidinium, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP) - EMEA/H/C/003969/WS1794/0029; DUAKLIR GENUAIR (CAP) - EMEA/H/C/003745/WS1794/0029

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from study D6570R00002 (listed as a category 3 study in the RMP): a descriptive, non-interventional, multinational European cohort study of new users of aclidinium, aclidinium/formoterol, and other selected chronic obstructive pulmonary disease (COPD) medications to describe the characteristics and patterns of use. As a consequence, the following safety concerns listed as missing information in the RMP are removed 'safety in patients with hepatic or severe renal impairment', 'safety in patients with benign hyperplasia or urinary retention' and 'use in pregnancy or lactation'. The RMP (version 5.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0017

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from study I4V-MC-B010 (listed as a category 3 study in the RMP): an observational, multinational cross-sectional survey amongst rheumatologists to assess the effectiveness of the risk minimisation measures (RMM) for Olumiant (baricitinib). The RMP (version 9.2) is updated accordingly. The MAH took the opportunity to remove from the RMP three safety concerns listed as missing information namely 'use in combination with biologic disease-modifying anti-rheumatic drugs (bDMARDs) or with other Janus kinase (JAK) inhibitors', 'use in patients with severe hepatic impairment', 'effect on fertility, on pregnancy and the foetus', and 'use in breastfeeding' as requested in the conclusions of variation II/006 finalised in July 2018

Action: For adoption of PRAC Assessment Report

7.4.4. Everolimus - AFINITOR (CAP) - EMEA/H/C/001038/WS1923/0068; VOTUBIA (CAP) - EMEA/H/C/002311/WS1923/0067

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report (CSR) for study CRAD001MIC03 (TOSCA): an international disease registry collecting data on manifestations, interventions and outcomes in patients with tuberous sclerosis complex (TSC). The RMP (version 15.0) is updated accordingly and in line with the conclusions of variation WS1671 adopted in October 2019

Action: For adoption of PRAC Assessment Report

7.4.5. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/WS1915/0091; sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/WS1915/0051; sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/WS1915/0043

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study GS-US-248-0123 (listed as a category 3 study in the RMP): a long-term observational follow-up registry of subjects who did not achieve sustained virologic response in Gilead-sponsored trials in subjects with chronic hepatitis C infection. The RMPs (Harvoni version 7.1, Epclusa version 6.1, Vosevi version 3.1) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. 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

7.4.7. Teriparatide - FORSTEO (CAP) - EMEA/H/C/000425/II/0054

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final report for the European Union (EU) component of study B3D-MC-GHBX(2.1): a registry to estimate the incidence of osteosarcoma in patients who have received treatment with Forsteo (teriparatide)

Action: For adoption of PRAC Assessment Report

7.4.8. 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. Adalimumab - IMRALDI (CAP) - EMEA/H/C/004279/MEA 003

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report of the safety surveillance programme using the Register for Antirheumatic Therapies in Sweden (ARTIS): a national prospective, observational, uncontrolled cohort study to evaluate the risk of selected adverse events (AEs) in rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA) and other rheumatic disease patients treated with adalimumab

Action: For adoption of advice to CHMP

7.5.2. Adalimumab - IMRALDI (CAP) - EMEA/H/C/004279/MEA 004

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual registry report of the safety surveillance programme using the Spanish Registry for Adverse Events for Biological Therapy in Rheumatic Diseases (BIOBASASER)

Action: For adoption of advice to CHMP

7.5.3. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.4

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a biennial report for study BEL115467/HGS1006-C1113: a randomized, double-blind placebo-controlled large safety study, based on a protocol agreed with CHMP, evaluating over a minimum of one year the incidence of all-cause mortality and adverse events of special interest (AESI) in patients with systemic lupus erythematosus receiving belimumab

Action: For adoption of advice to CHMP

7.5.4. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/MEA 003.1

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 003 [tenth annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry [final clinical study report (CSR) expected in December 2021]] as per the request for supplementary information (RSI) adopted in May 2020

Action: For adoption of advice to CHMP

7.5.5. Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/MEA 001.4

Applicant: Almirall S.A

PRAC Rapporteur: Annika Folin

Scope: Second annual interim results for study M-41008-40 (listed as a category 3 study in the RMP): an observational PASS in European psoriasis registers to evaluate the long-term safety of Skilarence (dimethyl fumarate) used for the treatment of patients with moderate to severe psoriasis [future due date(s): end of data collection: Q1 2027; final study report expected within a year of availability of the final data set]

Action: For adoption of advice to CHMP

7.5.6. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 007.5

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fifth annual report for study CNTO148ART4001: a pregnancy research initiative to study the exposure to golimumab during pregnancy in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers; together with the study summary results for the 2020 interval report for study CNTO148ART4001

Action: For adoption of advice to CHMP

7.5.7. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 026.8

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fifth progress report for study MK-8259-013, the ulcerative colitis (UC) Nordic registry: a non-interventional observational longitudinal PASS of Simponi (golimumab) in the treatment of UC using Nordic national health registries

Action: For adoption of advice to CHMP

7.5.8. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 004.8

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 004.7 [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]] as per the request for supplementary information (RSI) adopted in June 2020

Action: For adoption of advice to CHMP

7.5.9. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/MEA 003.5

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 003.4 [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]] as per the request for supplementary information (RSI) adopted in June 2020

Action: For adoption of advice to CHMP

7.5.10. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/MEA 004.6

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Yearly progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice [final report due date expected in 2020]

Action: For adoption of advice to CHMP

7.5.11. Simoctocog alfa - VIHUMA (CAP) - EMEA/H/C/004459/MEA 004.5

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Yearly progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice [final report due date expected in 2020]

Action: For adoption of advice to CHMP

7.5.12. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 018.4

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 018.3 [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]] as per the request for supplementary information (RSI) adopted in June 2020

Action: For adoption of advice to CHMP

7.5.13. Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/MEA 001.1

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 001 [interim analysis report for study MLN-0002-401 (listed as a category 3 study in the RMP): an international prospective, observational, cohort safety study comparing vedolizumab to other biologic agents in patients with ulcerative colitis or Crohn's disease [final clinical study report (CSR) expected in June 2022]] as per the request for supplementary information (RSI) adopted in July 2020

Action: For adoption of advice to CHMP

7.6. Others

None

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. Cerliponase alfa - BRINEURA (CAP) - EMEA/H/C/004065/S/0028 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/S/0083 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/S/0051 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Smallpox vaccine (live modified vaccinia virus Ankara) - IMVANEX (CAP) - EMEA/H/C/002596/S/0054 (without RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.5. Vestronidase alfa - MEPSEVII (CAP) - EMEA/H/C/004438/S/0017 (without RMP)

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Eva Segovia

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. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/R/0040 (without RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0023 (without RMP)

Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Albutrepenonacog alfa - IDELVION (CAP) - EMEA/H/C/003955/R/0047 (without RMP)

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Amlodipine, valsartan - AMLODIPINE-VALSARTAN MYLAN (CAP) - EMEA/H/C/004037/R/0008 (with RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/R/0077 (without RMP)

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Emtricitabine, rilpivirine, tenofovir alafenamide - ODEFSEY (CAP) - EMEA/H/C/004156/R/0049 (with RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Emtricitabine, tenofovir alafenamide - DESCOVY (CAP) - EMEA/H/C/004094/R/0051 (without RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/R/0064 (without RMP)

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Migalastat - GALAFOLD (CAP) - EMEA/H/C/004059/R/0027 (with RMP)

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Ulla Wändel Liminga

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

None

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

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.4.2. Coronavirus (COVID-19) pandemic – pharmacovigilance initiatives: preparedness plan and coverage data gathering

Action: For discussion

12.4.3. European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) steering group – Call for expression of interest for a PRAC representative

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q3 2020 and predictions

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.10.5. Union reference date (EURD) list: EURD tool - update

PRAC lead: Menno van der Elst

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. EudraVigilance – Expert Working Group (EV-EWG) - work programme 2021-2022

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Coronavirus (COVID-19) pandemic - coreRMP19 guidance and requirements for COVID-19 vaccines

PRAC lead: Jean-Michel Dogné, Birgitta Grundmark, Brigitte Keller-Stanislawski, Anette Kirstine Stark, Sabine Straus, Menno van der Elst, Ulla Wändel Liminga

Action: For adoption

12.14.2. Risk management systems

None

12.14.3. 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

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Good Pharmacovigilance Practice (GVP) - update on GVP status overview – planning for 2021

Action: For discussion

12.20.2. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact – Revised process for prioritising impact research topics

PRAC lead: Antoine Pariente

Action: For discussion

13. Any other business

14. Explanatory notes

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

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures
(Items 2 and 3 of the PRAC agenda)

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

Signals assessment and prioritisation
(Item 4 of the PRAC agenda)

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

Risk Management Plans (RMPs)
(Item 5 of the PRAC agenda)

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

Assessment of Periodic Safety Update Reports (PSURs)
(Item 6 of the PRAC agenda)

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

Post-authorisation Safety Studies (PASS)
(Item 7 of the PRAC agenda)

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

Product related pharmacovigilance inspections
(Item 9 of the PRAC agenda)

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

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