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Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 06-09 July 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

06 July 2020, 10:30 – 19:30, via teleconference

07 July 2020, 08:30 – 19:30, via teleconference

08 July 2020, 08:30 – 19:30, via teleconference

09 July 2020, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

23 July 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 06-09 July 2020. See July 2020 PRAC minutes (to be published post September 2020 PRAC meeting).

1.2. Agenda of the meeting on 06-09 July 2020

Action: For adoption

1.3. Minutes of the previous meeting on 08-11 June 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. Ifosfamide¹ (NAP) - EMEA/H/A-31/1495

Applicant(s): various

PRAC Rapporteur: Martin Huber; PRAC Co-rapporteur: Željana Margan Koletić

Scope: Review of the benefit-risk balance following notification by France of a referral under

¹ Solution, concentrate for solution

Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

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

3.2.2. Ulipristal acetate² – 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 discussion

3.3. Procedures for finalisation

None

3.4. Re-examination procedures³

None

3.5. Others

None

4. Signals assessment and prioritisation⁴

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Anakinra - KINERET (CAP); canakinumab – ILARIS (CAP)

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

PRAC Rapporteur: To be appointed

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

Action: For adoption of PRAC recommendation

EPITT 19566 – New signal

Lead Member State(s): DE, DK

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

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: To be appointed

² 5 mg

³ Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

⁴ 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

Scope: Signal of sarcoidosis
Action: For adoption of PRAC recommendation
EPITT 19574 – New signal
Lead Member State(s): NO, SE

4.1.3. Ibrutinib – IMBRUVICA (CAP)

Applicant(s): Janssen-Cilag International
PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: Signal of hepatitis E
Action: For adoption of PRAC recommendation
EPITT 19569 – New signal
Lead Member State(s): HR

4.1.4. Palbociclib - IBRANCE (CAP)

Applicant(s): Pfizer Europe MA EEIG
PRAC Rapporteur: Hans Christian Siersted
Scope: Signal of cutaneous lupus erythematosus
Action: For adoption of PRAC recommendation
EPITT 19571 – New signal
Lead Member State(s): DK

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Adalimumab - AMGEVITA (CAP); AMSPARITY (CAP), HALIMATOZ (CAP); HEFIYA (CAP); HULIO (CAP); HUMIRA (CAP) - EMEA/H/C/000481/SDA/118; HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP)

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Humira), Amgen Europe B.V. (Amgevita), Fresenius Kabi Deutschland GmbH (Idacio), Mylan S.A.S (Hulio), Pfizer Europe MA EEIG (Amsparity), Samsung Bioepis NL B.V. (Imraldi), Sandoz GmbH (Halimatoz, Hefiya, Hyrimoz)
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Signal of abnormal weight gain
Action: For adoption of PRAC recommendation
EPITT 19520 – Follow-up to February 2020

4.3.2. Lisdexamfetamine (NAP)

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of QT prolongation and cardiac arrhythmia

Action: For adoption of PRAC recommendation

EPITT 19533 – Follow-up to February 2020

4.3.3. Lopinavir, ritonavir – ALUVIA (Art 58⁵) - EMEA/H/W/000764/SDA/033, KALETRA (CAP) - EMEA/H/C/000368/SDA/123, LOPINAVIR/RITONAVIR MYLAN (CAP); NAP

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Aluvia, Kaletra), Mylan S.A.S (Lopinavir, Ritonavir Mylan), various

PRAC Rapporteur: Adrien Inoubli

Scope: Signal of adrenal dysfunction in infants

Action: For adoption of PRAC recommendation

EPITT 19527 – Follow-up to March 2020

4.3.4. Teriparatide - FORSTEO (CAP) - EMEA/H/C/000425/SDA/052, MOVYMIA (CAP) - EMEA/H/C/004368/SDA/002; TERROSA (CAP) - EMEA/H/C/003916/SDA/002; NAP

Applicant(s): Eli Lilly Nederland B.V. (Forsteo), Gedeon Richter Plc. (Terrosa), Stada Arzneimittel AG (Movymia), various

PRAC Rapporteur: Adrien Inoubli

Scope: Signal of myeloma

Action: For adoption of PRAC recommendation

EPITT 19511 – Follow-up to February 2020

4.3.5. Tumour necrosis factor (TNF) inhibitors: adalimumab - AMGEVITA (CAP), AMSPARITY (CAP), HALIMATOZ (CAP), HEFIYA (CAP), HULIO (CAP), HUMIRA (CAP) - EMEA/H/C/000481/SDA/120, HYRIMOZ (CAP), IDACIO (CAP), IMRALDI (CAP); certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/SDA/039; etanercept - BENEPALI (CAP), ENBREL (CAP) - EMEA/H/C/000262/SDA/173, ERELZI (CAP); golimumab - SIMPONI (CAP) - EMEA/H/C/000992/SDA/036; infliximab - FLIXABI (CAP), INFLECTRA (CAP), REMICADE (CAP) - EMEA/H/C/000240/SDA/158, REMSIMA (CAP), ZESSLY (CAP)

Applicant(s): AbbVie Deutschland GmbH Co. KG (Humira), Amgen Europe B.V. (Amgevita), Celltrion Healthcare Hungary Kft. (Remsima), Fresenius Kabi Deutschland GmbH (Idacio), Mylan S.A.S. (Hulio), Janssen Biologics B.V. (Simponi, Remicade), Pfizer Europe MA EEIG (Amsparity, Enbrel, Inflectra), Samsung Bioepis NL B.V. (Benepali, Flixabi, Imraldi), Sandoz GmbH (Erelzi, Halimatoz, Hefiya, Hyrimoz, Zessly), UCB Pharma S.A. (Cimzia)

PRAC Rapporteur: Ulla Wändel Liminga

⁵ Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

Scope: Signal of Kaposi's sarcoma

Action: For adoption of PRAC recommendation

EPITT 19480 – Follow-up to April 2020

4.4. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Cabotegravir - EMEA/H/C/004976

Scope: Treatment of human immunodeficiency virus type 1 (HIV-1)

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

5.1.2. Influenza quadrivalent vaccine (rDNA⁶) - EMEA/H/C/005159

Scope: Prevention of influenza disease

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

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

Applicant: EigerBio Europe Limited

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

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

5.1.4. Lumasiran - EMEA/H/C/005040, Orphan

Applicant: Alnylam Netherlands B.V.

Scope (accelerated assessment): Treatment of primary hyperoxaluria type 1 (PH1)

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

5.1.5. Meningococcal group A, C, W-135 and Y conjugate vaccine - EMEA/H/C/005084

Scope: Immunisation against Neisseria meningitidis serogroups A, C, W-135 and Y

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

5.1.6. Rilpivirine - EMEA/H/C/005060

Scope: Treatment of human immunodeficiency virus type 1 (HIV-1)

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

⁶ Ribosomal deoxyribonucleic acid

5.2. Medicines in the post-authorisation phase – PRAC-led procedures

5.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/II/0031

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 7.0) in order to reflect all amendments and additional activities as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in November 2019 (EMEA/H/A-20/1483)

Action: For adoption of PRAC Assessment Report

5.2.2. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS1844/0039; FORXIGA (CAP) - EMEA/H/C/002322/WS1844/0057

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Re-categorisation of study D169C00011: a retrospective cohort study on the risk of diabetic ketoacidosis (DKA) to determine the effectiveness of additional risk minimisation measures (aRMMs) in place for DKA by assessing the impact of the risk minimisation measures (RMMs) on the risk of DKA in type 1 diabetes mellitus (T1DM) patients who are treated with dapagliflozin in Europe, from a category 1 to a category 3 study in the RMP (version 20). Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.3. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/II/0031

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Submission of an updated RMP (version 3.0) to reflect a potential increased risk of exacerbation of pre-existing potentially immune-mediated diseases (pIMDs) following vaccination with Shingrix (herpes zoster vaccine (recombinant, adjuvanted)). The implementation of the change is further substantiated by new additional data on post-hoc analyses and spontaneous reports of potential exacerbations of pIMDS from a worldwide safety database

Action: For adoption of PRAC Assessment Report

5.2.4. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0080

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 28.0) in order to propose the discontinuation of the healthcare professional adverse reaction management guide as an additional risk minimisation measure (aRMM). Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly. The

MAH took the opportunity to bring in line the product information with the latest quality review of documents (QRD) template (version 10.1) and in line with the latest Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' on sodium content

Action: For adoption of PRAC Assessment Report

5.2.5. [Tacrolimus - ADVAGRAF \(CAP\) - EMEA/H/C/000712/WS1805/0057](#); [MODIGRAF \(CAP\) - EMEA/H/C/000954/WS1805/0035](#)

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 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 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.6. [Umeclidinium, vilanterol - ANORO ELLIPTA \(CAP\) - EMEA/H/C/002751/WS1850/0030](#); [LAVENTAIR ELLIPTA \(CAP\) - EMEA/H/C/003754/WS1850/0033](#)

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of an updated RMP (version 8.2) 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

Action: For adoption of PRAC Assessment Report

5.2.7. [Umeclidinium - INCRUSE ELLIPTA \(CAP\) - EMEA/H/C/002809/WS1589/0029](#); [ROLUFTA ELLIPTA \(CAP\) - EMEA/H/C/004654/WS1589/0014](#)

Applicant: GlaxoSmithKline (Ireland) Limited

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

5.2.8. Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/II/0050

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of an updated RMP (version 6.0) with regards to the measures to evaluate the effectiveness of the patient alert card as an additional risk minimisation measure (aRMM). The MAH took the opportunity to add the completion date of the interim report for study MLN0002_401: an international observational prospective cohort study comparing vedolizumab to other biologic agents in patients with ulcerative colitis or Crohn's disease

Action: For adoption of PRAC Assessment Report

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

5.3.1. Adalimumab - HULIO (CAP) - EMEA/H/C/004429/X/0016

Applicant: Mylan S.A.S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to add a new strength of 20 mg solution for injection. The RMP (version 3.1) is updated in accordance

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

5.3.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0198

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of moderately to severely active ulcerative colitis in paediatric patients. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC for the 40mg/0.8mL, 40mg/0.4mL and 80mg/0.8mL presentations are updated. Furthermore, sections 5.1 and 5.2 of the SmPC for the 20mg/0.2mL presentation are updated. The package leaflet and the RMP (version 15.0) are updated in accordance

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

5.3.3. [Albutrepenonacog alfa - IDELVION \(CAP\) - EMEA/H/C/003955/II/0042, Orphan](#)

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.2 of the SmPC to update the posology by expanding the once weekly routine prophylaxis regimen from 35-to 50 IU/kg to 25- to 50 IU/kg. The RMP (version 3.3) is updated accordingly

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

5.3.4. [Avelumab - BAVENCIO \(CAP\) - EMEA/H/C/004338/II/0015](#)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to change posology recommendations, to amend an existing warning and to add myasthenia gravis and myasthenic syndrome as new adverse drug reactions (ADRs) with a frequency uncommon. The update results from an update of the company core data sheet (CCDS) based on the review of cases of myasthenia gravis/myasthenic syndrome. The package leaflet is updated accordingly. The RMP (version 2.2) is updated with a proposal to reclassify 'other immune-related events (myasthenic syndrome)' from an important potential risk to an important identified risk of 'other immune-related events (myasthenia gravis/myasthenic syndrome)'

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

5.3.5. [Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - TRIMBOW \(CAP\) - EMEA/H/C/004257/X/0012](#)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension application to add a new pharmaceutical form (inhalation powder) associated with a new strength (88µg/5µg/9µg). The RMP (version 6.2) is updated in accordance

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

5.3.6. [Bortezomib - BORTEZOMIB FRESENIUS KABI \(CAP\) - EMEA/H/C/005074/II/0001/G](#)

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Grouped variations consisting of: 1) addition of a new pack size (EU number-EU/1/19/1397/002) for the sterile parenteral biological medicinal product Bortezomib Fresenius Kabi (bortezomib) powder for solution for injection with a fill volume for a single dose vial of 1 mg per vial in addition to the authorised 3.5 mg per vial; 2) addition of a new pack size within a range (EU number-EU/1/19/1397/003) for the sterile parenteral biological medicinal product Bortezomib Fresenius Kabi (bortezomib) powder for solution for injection with a fill volume for a single dose vial of 2.5 mg per vial in addition to the authorised 3.5 mg per vial. The RMP (version 2.0) is updated accordingly

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

5.3.7. [Cannabidiol - EPIDYOLEX \(CAP\) - EMEA/H/C/004675/II/0005, Orphan](#)

Applicant: GW Pharma (International) B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication for use as adjunctive therapy of seizures associated with tuberous sclerosis complex (TSC) for patients 1 year of age and older. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly. The MAH took the opportunity to correct typographic errors in the product information, to introduce editorial updates and to implement the updated ethanol statement in compliance 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

5.3.8. [Catridecacog - NOVOTHIRTEEN \(CAP\) - EMEA/H/C/002284/II/0026/G](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped variations consisting of an extension of indication to include treatment of bleeding episodes in patients with congenital factor XIII A-subunit deficiency as well as minor surgery based on the results of: 1) study NN1841-3868: use of recombinant factor XIII (rFXIII) in treatment of congenital FXIII deficiency, a prospective multi-centre observational study; 2) registry PRO-RBDD: a prospective rare bleeding disorders database registry. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPC are updated. The package leaflet, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 15) are 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 minor editorial changes to the product information

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

5.3.9. [Ceftazidime, avibactam - ZAVICEFTA \(CAP\) - EMEA/H/C/004027/II/0015](#)

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to include paediatric patients aged 3 months to less than 18 years for Zavicefta (ceftazidime/avibactam) based on data from three paediatric studies namely, study D4280C00014: a phase 1 study to assess the pharmacokinetics, safety and tolerability of a single dose of ceftazidime-avibactam (CAZ-AVI) in children from 3 months of age to <18 years who are receiving systemic antibiotic therapy for suspected or confirmed infection; study C3591004: a single blind, randomised, multicentre, active controlled, trial to evaluate safety, tolerability, pharmacokinetics (PK) and efficacy of ceftazidime and avibactam when given in combination with metronidazole, compared with meropenem, in children from 3 months to less than 18 years of age with complicated intra-

abdominal infections (cIAIs); and study C3591005: a single blind, randomised, multicentre, active controlled, trial to evaluate safety, tolerability, pharmacokinetics and efficacy of ceftazidime and avibactam compared with cefepime in children from 3 months to less than 18 years of age with complicated urinary tract infections (CUTIs); as well as population PK modelling/simulation analyses (CAZ-MS-PED-01 and CAZ-MS-PED-02). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.3 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to correct sections 2 and 4.4 of the SmPC and the package leaflet with information on sodium content, as well as section 5.2 of the SmPC with information on volumes of distribution of ceftazidime and avibactam. Furthermore, the MAH also introduced minor correction in the Czech product information

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

5.3.10. [Dabigatran etexilate - PRADAXA \(CAP\) - EMEA/H/C/000829/X/0122/G](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped applications consisting of: 1) extension application to add two new pharmaceutical forms coated granules (20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg) and powder and solvent for oral solution (6.25 mg/mL); 2) extension of indication to include treatment of venous thromboembolic events (VTE) and prevention of recurrent VTE in paediatric patients from birth to less than 18 years of age for Pradaxa (dabigatran etexilate) 75 mg, 110 mg, 150 mg capsules based on paediatric trials, namely study 1160.106: an open-label, randomized, parallel-group, active-controlled, multi-centre non-inferiority study of dabigatran etexilate versus standard of care for venous thromboembolism treatment in children from birth to less than 18 years of age, and study 1160.108: an open label, single arm safety prospective cohort study of dabigatran etexilate for secondary prevention of venous thromboembolism in children from 0 to less than 18 years. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and labelling are updated in accordance. The RMP (version 37.0) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.11. [Darunavir - PREZISTA \(CAP\) - EMEA/H/C/000707/II/0107](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of indication for Prezista (darunavir) 800 mg in combination with cobicistat (COBI) 150 mg for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adolescents aged 12 years and older with a body weight of at least 40 kg. 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 27.1) are updated accordingly

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

5.3.12. Desloratadine - DESLORATADINE RATIOPHARM (CAP) - EMEA/H/C/002404/II/0023/G

Applicant: Ratiopharm GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Grouped variations consisting of: 1) change in the legal status of Desloratadine ratiopharm from 'medicinal product subject to medical prescription' to 'medicinal product not subject to medical prescription' in view of the safety profile of Desloratadine ratiopharm and the post-marketing experience already available with other medicinal products containing similar long acting histamine antagonists. The RMP (version 1.0) is updated accordingly. In addition, the MAH also took the opportunity to bring the product information (PI) in line with the latest quality review of documents (QRD) template (version 10.1), to update the list of local representatives in the package leaflet and to introduce editorial changes.; 2) deletion of the therapeutic indication in adolescents aged 12 years and older for the relief of symptoms associated with allergic rhinitis and urticaria. As a consequence, section 4.1 of the SmPC is updated. The package leaflet is updated accordingly

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

5.3.13. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/X/0045

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Extension application to introduce two new strengths of 3 mg and 4.5 mg solution for injection. The RMP (version 4.1) is updated accordingly

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

5.3.14. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0027

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include atopic dermatitis patients from 6 years to 11 years. 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 5.0) are updated accordingly

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

5.3.15. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/II/0022

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Extension of indication to include adults of 18 years of age or older at increased risk of herpes zoster, supported by clinical studies: 1) study ZOSTER-002: a phase 3, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the prophylactic efficacy, safety, and immunogenicity of Shingrix (herpes zoster vaccine) when administered intramuscularly on a two-dose schedule to adult autologous haematopoietic stem cell transplant (HCT) recipients (MEA 001); 2) study ZOSTER-039: a phase 3,

randomised, observer-blind, placebo-controlled, multicentre study to assess the safety and immunogenicity of Shingrix (herpes zoster vaccine) when administered intramuscularly on a two-dose schedule to adults aged 18 years and older with haematologic malignancies (MEA 002); 3) study ZOSTER-041: a phase 3, randomised, observer-blind, placebo-controlled, multicentre clinical study to assess the immunogenicity and safety of Shingrix (herpes zoster vaccine) when administered intramuscularly on a 0- and 1- to 2-months schedule to adults \geq 18 years of age with renal transplant (MEA 003); 4) study ZOSTER-028: a phase 2/3, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of Shingrix (herpes zoster vaccine) when administered intramuscularly on a 0 and 1 to 2 months schedule to adults of 18 years of age with solid tumours receiving chemotherapy (MEA 004); 5) study ZOSTER-001: a phase 1/2a, randomised, observer-blind, placebo-controlled, multicentre study to evaluate the safety and immunogenicity of Shingrix (herpes zoster vaccine) and to saline (placebo) when administered as 2 doses or 3 doses to autologous HCT recipients ; 6) study ZOSTER-015: a phase 1/2a, randomised, observer-blind, placebo-controlled, multicentre study to evaluate the safety and immunogenicity of Shingrix (herpes zoster vaccine) in comparison to placebo when administered as 3 doses to adult human immunodeficiency virus (HIV)-infected subjects.. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated in order to add the indication, delete a warning and add new safety and efficacy information. 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

5.3.16. Human normal immunoglobulin - HYQVIA (CAP) - EMEA/H/C/002491/II/0056

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to replace the therapeutic indications of replacement therapy in hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia and multiple myeloma and hypogammaglobulinaemia in patients with hematopoietic stem cell transplantation (HSCT), by the therapeutic indication of replacement therapy in secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either proven specific antibody failure (PSAF) or serum immunoglobulin G (IgG) level of <4 g/L. As a consequence, sections 4.1 and 4.2 of the SmPC are updated. The package leaflet and the RMP (version 10.0) are updated in accordance

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

5.3.17. Human normal immunoglobulin - PRIVIGEN (CAP) - EMEA/H/C/000831/II/0161/G

Applicant: CSL Behring GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) update of sections 4.4, 4.8 and 5.1 of the SmPC in order to amend an existing warning on haemolytic anaemia and to update safety information based on final results from study IgPro10_5003 (listed as a category 3 study in the RMP): an observational hospital-based cohort study in the US to evaluate Privigen (human normal immunoglobulin) use and haemolytic anaemia in adults and children and the Privigen (human normal immunoglobulin) safety profile in children with chronic

inflammatory demyelinating polyneuropathy (CIDP). The package leaflet is updated accordingly; 2) update of sections 4.8 and 5.1 of the SmPC in order to update the list of adverse drug reactions based on final results from study IgPro10_3004: a prospective open-label single-arm study of the pharmacokinetics and safety of intravenous IgPro10 in Japanese subjects with primary immunodeficiency. The RMP (version 8.0) is updated accordingly. In addition, the MAH took the opportunity to align the SmPC with the EU core SmPC for human normal immunoglobulin for intravenous administration (IVIg) (EMA/CHMP/BPWP/94038/2007 Rev. 5), to update the local representative for Bulgaria in the package leaflet and 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

5.3.18. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0059, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to add the combination with rituximab or obinutuzumab for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL), based on results from study E1912 (PCYC-1126e-CA): a randomized phase 3 study of ibrutinib-based therapy vs standard fludarabine, cyclophosphamide, and rituximab (FCR) chemo-immunotherapy in untreated younger patients with CLL. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated to include information related to the new indication. The package leaflet and the RMP (version 16.1) are updated accordingly. The MAH took the opportunity to introduce minor editorial changes in Annex II and the labelling (Annex III-A)

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

5.3.19. Imipenem, cilastatin, relebactam - RECARBRIO (CAP) - EMEA/H/C/004808/II/0001

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include the treatment of hospital-acquired pneumonia (HAP) including ventilator-associated pneumonia (VAP), with or without concurrent bacteraemia in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet and the RMP (version 1.1) are updated in accordance. Furthermore, the MAH introduced editorial corrections in the product information and brought it in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.20. Insulin glargine - ABASAGLAR (CAP) - EMEA/H/C/002835/WS1587/0028/G; insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/WS1587/0178/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of: 1) introduction of an additional prefilled pen

presentation for Abasaglar (insulin glargine), solution for injection, Humalog (insulin lispro) solution for injection, Humalog (insulin lispro) Kwikpen solution for injection and Humalog (insulin lispro) Junior Kwikpen solution for injection. Each pack contains 5 pre-filled pens; 2) extension to two x5 multipacks. As a consequence, sections 1, 4.2, 4.4, 6.2, 6.4, 6.5, 6.6 and 8 of the SmPC are updated. The package leaflet and labelling are updated accordingly. In addition, the MAH took the opportunity to introduce an editorial change in the Slovakian address of the package leaflet

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/II/0085, Orphan](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include the combination regimen of the ivacaftor 150 mg tablets with elexacaftor/tezacaftor/ivacaftor fixed dose combination (FDC) tablets for the treatment of adults and adolescents aged 12 years and older with cystic fibrosis who have at least one phenylalanine in position 508 deletion (F508del) mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 8.8) are updated in accordance

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

5.3.22. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/II/0086, Orphan](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to extend the indication of Kalydeco (ivacaftor) granules in the treatment of infants aged at least 4 months, toddlers and children weighing 5 kg to less than 25 kg with cystic fibrosis who have one of the following gating (class III) mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 8.9) are updated in accordance

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

5.3.23. [Lacosamide - LACOSAMIDE UCB \(CAP\) - EMEA/H/C/005243/WS1782/0006; VIMPAT \(CAP\) - EMEA/H/C/000863/WS1782/0088](#)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment as adjunctive therapy of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy. 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 15.1) 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), to align the

product information of Lacosamide UCB (lacosamide) with the product information of Vimpat (lacosamide) and to implement some minor corrections in the Bulgarian, Czech, Danish, French, German, Hungarian, Polish and Spanish versions of the product information

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

5.3.24. [Levetiracetam - KEPBRA \(CAP\) - EMEA/H/C/000277/WS1664/0187](#)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Update of section 4.2 of the SmPC to recommend the same dosing for monotherapy and adjunctive therapy based on data from modelling and simulation project. The package leaflet and the RMP (version 9.1) are updated accordingly. The MAH took the opportunity to move Braille to another box section and to review and adapt the German 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

5.3.25. [Lumacaftor, ivacaftor - ORKAMBI \(CAP\) - EMEA/H/C/003954/II/0055](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of section 4.8 of the SmPC following results from study VX16-809-116 (study 106, safety study in children): a phase 3, open-label, rollover extension study evaluating the long-term safety of lumacaftor/ivacaftor in patients with cystic fibrosis aged 2 and older, homozygous for the deletion of phenylalanine in position 508 of the cystic fibrosis transmembrane conductance regulator (F508del-CFTR) mutation, who initiated treatment in parent study 115. The package leaflet and the RMP (version 7.1) are updated accordingly. The 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

5.3.26. [Meningococcal group B vaccine \(recombinant, adsorbed\) - TRUMENBA \(CAP\) - EMEA/H/C/004051/II/0027/G](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Grouped variations consisting of: 1) a revised protocol outline for study B1971060: a phase 4, open-label, single-arm trial, to describe the safety, tolerability and immunogenicity of Trumenba (meningococcal group B vaccine/bivalent rLP2086 vaccine) when administered in immunocompromised subjects ≥ 10 years of age in order to change from a 3 dose-regimen of Trumenba (meningococcal group B vaccine) administered on a 0-, 2-, and 6-month schedule to a 2-dose regimen administered on 0- and 6-month schedule; 2) a proposal to replace study B1971062 aimed at investigating the co-administration of Trumenba (meningococcal group B vaccine) with measles, mumps, and rubella (MMR) and pneumococcal vaccines, with study C3511006 (MenABCWY): a phase 2b, randomised, controlled, open-label trial to describe the safety, tolerability, and immunogenicity of

bivalent rLP2086-containing MenABCWY when administered concomitantly with MMR and 13-valent pneumococcal vaccine (13vPnC) in healthy participants ≥ 12 to < 16 months of age. A protocol outline is included. The RMP (version 4.0) is updated accordingly

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

5.3.27. Metreleptin - MYALEPTA (CAP) - EMEA/H/C/004218/II/0012, Orphan

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 4.4 of the SmPC in order to add a new warning on the risk of autoimmune disease following exposure to metreleptin. The package leaflet and the key elements to be included in the guide/training material for healthcare professionals are updated accordingly. The RMP (version 2.0) is also updated in accordance

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

5.3.28. 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 (solution for injection), associated with a new strength (150 mg) and a new route of administration (subcutaneous use). The RMP (version 26.1) is updated accordingly

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

5.3.29. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0080

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) after prior fluoropyrimidine- and platinum-based chemotherapy. 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 16.0) are updated in accordance

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

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

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wandel Liminga

Scope: Grouped applications consisting of: 1) extension application to introduce a new pharmaceutical form, granules for oral suspension, 1 mg/mL; 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 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

5.3.31. Sebelipase alfa - KANUMA (CAP) - EMEA/H/C/004004/II/0026/G, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the clinical information based on the pooled safety and efficacy analysis of already submitted studies (namely study LAL-CL04: an open label multicentre extension study to evaluate the long-term safety, tolerability, and efficacy of sebelipase alfa (SBC-102) in adult subjects with liver dysfunction due to lysosomal acid lipase deficiency (LAL-D) who previously received treatment in study LAL-CL01; study LAL-CL03: an open label, multicentre, dose escalation study to evaluate the safety, tolerability, efficacy, pharmacokinetics, and pharmacodynamics of SBC-102 in children with growth failure due to LAL-D; study LAL-CL06: a multicentre, open-label study of sebelipase alfa in patients with LAL-D; study LAL-CL08: a phase 2, open label, multicentre study to evaluate the safety, tolerability, efficacy, and pharmacokinetics of sebelipase alfa in infants with rapidly progressive LAL-D; study LAL-CL02: a multicentre, randomized, placebo-controlled study of SBC-102 in patients with LAL-D) and updated population pharmacokinetic (PK) analyses in children and adults. The package leaflet and the RMP (version 4.0) are updated accordingly. Annex II is also updated to remove the obligation related to the provision of study LAL-CL08; 2) submission of the final report from study LAL-EA01: an open-label study with sebelipase alfa 1 mg/kg every other week for up to 78 weeks or until drug commercialisation in the United States (US) patients who did not otherwise qualify for an active sebelipase alfa trial (expanded access protocol)

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

5.3.32. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0097

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.2 of the SmPC for the 20 mg/mL concentrate for solution for infusion presentation in order to amend the existing recommendations for monitoring of laboratory abnormalities in systemic juvenile idiopathic arthritis (sJIA) patients based on final results from study WA28029 (ARTHUR) (listed as a category 3 study in the RMP): a phase 4 study to evaluate decreased dose frequency in sJIA who experience laboratory abnormalities during treatment with tocilizumab. The RMP (version 26.0) is updated in accordance and also reflects the completion of study WA22480 (ARTIS) as assessed in variation II/0094 finalised in May 2020

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. Aflibercept⁷ - EYLEA (CAP) - PSUSA/00010020/201911

Applicant: Bayer AG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Allopurinol, lesinurad - DUZALLO (CAP) - PSUSA/00010704/201912

Applicant: Grunenthal GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Angiotensin II - GIAPREZA (CAP) - PSUSA/00010785/201912

Applicant: La Jolla Pharmaceutical II B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Betibeglogene autotemcel - ZYNTEGLO (CAP) - PSUSA/00010769/201911

Applicant: Bluebird bio (Netherlands) B.V, ATMP⁸

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.5. Binimetinib - MEKTOVI (CAP) - PSUSA/00010717/201912

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

⁷ Ophthalmological indication(s) only

⁸ Advanced therapy medicinal product

6.1.6. [Blinatumomab - BLINCYTO \(CAP\) - PSUSA/00010460/201912](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. [Cannabidiol⁹ - EPIDYOLEX \(CAP\) - PSUSA/00010798/201912](#)

Applicant: GW Pharma (International) B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. [Dengue tetravalent vaccine \(live, attenuated\) - DENGIVAXIA \(CAP\) - PSUSA/00010740/201912](#)

Applicant: Sanofi Pasteur

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. [Dimethyl fumarate¹⁰ - SKILARENCE \(CAP\) - PSUSA/00010647/201912](#)

Applicant: Almirall S.A

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. [Elotuzumab - EMLICITI \(CAP\) - PSUSA/00010500/201911](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. [Encorafenib - BRAFTOVI \(CAP\) - PSUSA/00010719/201912](#)

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

⁹ Centrally authorised product(s) only

¹⁰ Indicated for the treatment of psoriasis

Action: For adoption of recommendation to CHMP

6.1.12. Ertugliflozin - STEGLATRO (CAP) - PSUSA/00010682/201912

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Ertugliflozin, metformin - SEGLUROMET (CAP); ertugliflozin, sitagliptin - STEGLUJAN (CAP) - PSUSA/00010784/201912

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Ethinylestradiol, norelgestromin - EVRA (CAP) - PSUSA/00001311/201911

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Follitropin delta - REKOVELLE (CAP) - PSUSA/00010554/201911

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Hydroxocobalamin¹¹ - CYANOKIT (CAP) - PSUSA/00010228/201911

Applicant: SERB SA

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Indacaterol - HIROBRIZ BREEZHALER (CAP); ONBREZ BREEZHALER (CAP); OSLIF BREEZHALER (CAP) - PSUSA/00001730/201911

Applicant: Novartis Europharm Limited

¹¹ Indicated for the treatment of chemical poisoning only

PRAC Rapporteur: Hans Christian Siersted
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.18. Inotuzumab ozogamicin - BESPONSA (CAP) - PSUSA/00010659/201912

Applicant: Pfizer Europe MA EEIG
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.19. Lesinurad - ZURAMPIC (CAP) - PSUSA/00010470/201912

Applicant: Grunenthal GmbH
PRAC Rapporteur: Eva Segovia
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.20. Levodopa - INBRIJA (CAP) - PSUSA/00107800/201912

Applicant: Acorda Therapeutics Ireland Limited
PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.21. Liraglutide - SAXENDA (CAP); VICTOZA (CAP) - PSUSA/00001892/201912

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

6.1.22. Lutetium (¹⁷⁷Lu) oxodotreotide - LUTATHERA (CAP) - PSUSA/00010643/201912

Applicant: Advanced Accelerator Applications
PRAC Rapporteur: Adam Przybylkowski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.23. Lutropin alpha - LUVERIS (CAP) - PSUSA/00001918/201911

Applicant: Merck Europe B.V.
PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.24. Mexiletine¹² - NAMUSCLA (CAP) - PSUSA/00010738/201912

Applicant: Lupin Europe GmbH
PRAC Rapporteur: Eva Jirsová
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.25. Netarsudil - RHOKIINSA (CAP) - PSUSA/00107812/201912

Applicant: Aerie Pharmaceuticals Ireland Ltd
PRAC Rapporteur: Eva Segovia
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.26. Nonacog beta pegol - REFIXIA (CAP) - PSUSA/00010608/201911

Applicant: Novo Nordisk A/S
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.27. Nusinersen - SPINRAZA (CAP) - PSUSA/00010595/201911

Applicant: Biogen Netherlands B.V.
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.28. Olaparib - LYNPARZA (CAP) - PSUSA/00010322/201912

Applicant: AstraZeneca AB
PRAC Rapporteur: Amelia Cupelli
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.29. Pegvisomant - SOMAVERT (CAP) - PSUSA/00002328/201911

Applicant: Pfizer Europe MA EEIG
PRAC Rapporteur: Adrien Inoubli

¹² Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.30. Peramivir - ALPIVAB (CAP) - PSUSA/00010687/201912

Applicant: BioCryst Ireland Limited
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.31. Pneumococcal polysaccharide conjugate vaccine (adsorbed)¹³ - SYNFLORIX (CAP) - PSUSA/00009262/201912

Applicant: GlaxoSmithkline Biologicals SA
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.32. Ponatinib - ICLUSIG (CAP) - PSUSA/00010128/201912

Applicant: Incyte Biosciences Distribution B.V.
PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.33. Ravulizumab - ULTOMIRIS (CAP) - PSUSA/00010787/201912

Applicant: Alexion Europe SAS
PRAC Rapporteur: Kimmo Jaakkola
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.34. Rucaparib - RUBRACA (CAP) - PSUSA/00010694/201912

Applicant: Clovis Oncology Ireland Limited
PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.35. Saquinavir - INVIRASE (CAP) - PSUSA/00002684/201912

Applicant: Roche Registration GmbH

¹³ 10-valent

PRAC Rapporteur: Jan Neuhauser
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.36. Secukinumab - COSENTYX (CAP) - PSUSA/00010341/201912

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Eva Segovia
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.37. Selexipag - UPTRAVI (CAP) - PSUSA/00010503/201912

Applicant: Janssen-Cilag International N.V.
PRAC Rapporteur: Adrien Inoubli
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.38. Semaglutide - OZEMPIC (CAP) - PSUSA/00010671/201911

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

6.1.39. Sofosbuvir - SOVALDI (CAP) - PSUSA/00010134/201912

Applicant: Gilead Sciences Ireland UC
PRAC Rapporteur: Ana Sofia Diniz Martins
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.40. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/201912

Applicant: Sun Pharmaceutical Industries Europe B.V.
PRAC Rapporteur: Željana Margan Koletić
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.41. Treosulfan¹⁴ - TRECONDI (CAP) - PSUSA/00010777/201912

Applicant: Medac Gesellschaft für klinische Spezialpräparate mbH

¹⁴ Centrally authorised product(s) only

PRAC Rapporteur: Julia Pallos
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.42. Turoctocog alfa pegol - ESPEROCT (CAP) - PSUSA/00010782/201912

Applicant: Novo Nordisk A/S
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.43. Ustekinumab - STELARA (CAP) - PSUSA/00003085/201912

Applicant: Janssen-Cilag International NV
PRAC Rapporteur: Rhea Fitzgerald
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.44. Venetoclax - VENCLYXTO (CAP) - PSUSA/00010556/201912

Applicant: AbbVie Deutschland GmbH & Co. KG
PRAC Rapporteur: Eva Jirsová
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.45. Vonigocog alfa - VEYVONDI (CAP) - PSUSA/00010714/201912

Applicant: Baxalta Innovations GmbH
PRAC Rapporteur: Ulla Wändel Liminga
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. Clofarabine - EVOLTRA (CAP); IVOZALL (CAP); NAP - PSUSA/00000805/201912

Applicants: Genzyme Europe BV (Evoltra), Orphelia Pharma SAS (Ivozall), various
PRAC Rapporteur: Tiphaine Vaillant
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.2.2. Clopidogrel - CLOPIDOGREL ZENTIVA (CAP), ISCOVER (CAP), PLAVIX (CAP); DUOPLAVIN (CAP); NAP - PSUSA/00000820/201911

Applicants: Sanofi-aventis groupe (DuoPlavin, Iscover, Plavix), Zentiva k.s. (Clopidogrel Zentiva), various

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Docetaxel - DOCETAXEL ZENTIVA (CAP); TAXOTERE (CAP); NAP - PSUSA/00001152/201911

Applicants: Sanofi Mature IP (Taxotere), Zentiva, k.s. (Docetaxel Zentiva), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Edotreotide - SOMAKIT TOC (CAP); NAP - PSUSA/00010552/201912

Applicants: Advanced Accelerator Applications (SomaKit TOC), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Erlotinib - TARCEVA (CAP); NAP - PSUSA/00001255/201911

Applicants: Roche Registration GmbH (Tarceva), various

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Lenalidomide - LENALIDOMIDE ACCORD (CAP); REVLIMID (CAP); NAP - PSUSA/00001838/201912

Applicants: Accord Healthcare S.L.U. (Lenalidomide Accord), Celgene Europe BV (Revlimid), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.7. Lutetium (¹⁷⁷Lu) chloride - ENDOLUCINBETA (CAP); LUMARK (CAP); NAP - PSUSA/00010391/201912

Applicants: I.D.B. Holland B.V. (Lumark), ITG Isotope Technologies Garching GmbH

(EndolucinBeta), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.8. [Riluzole - RILUTEK \(CAP\); RILUZOLE ZENTIVA \(CAP\); NAP - PSUSA/00002645/201912](#)

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

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.3. [PSUR single assessment \(PSUSA\) procedures including nationally authorised products \(NAPs\) only](#)

6.3.1. [Anthrax vaccine \(NAP\) - PSUSA/00010771/201912](#)

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. [Apomorphine \(NAP\) - PSUSA/00000227/201911](#)

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. [Bacillus clausii multi-antibioresistant spores \(NAP\) - PSUSA/00000284/201911](#)

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. [Brotizolam \(NAP\) - PSUSA/00000444/201912](#)

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. Chloroquine phosphate, proguanil hydrochloride (NAP) - PSUSA/00010207/201911

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Cinolazepam (NAP) - PSUSA/00000769/201912

Applicant(s): various

PRAC Lead: Marek Juračka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Dienogest (NAP) - PSUSA/00003167/201912

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Domperidone (NAP) - PSUSA/00001158/201911

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Drospirenone, estradiol (NAP) - PSUSA/00001184/201912

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Flurbiprofen (NAP) - PSUSA/00001450/201911

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Human coagulation factor VIII¹⁵ (NAP) - PSUSA/00001620/201911

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Hydroxycarbamide¹⁶ (NAP) - PSUSA/00009182/201912

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Idarubicin (NAP) - PSUSA/00001720/201911

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Iron¹⁷ (NAP) - PSUSA/00010236/202001

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Iron dextran (NAP) - PSUSA/00010696/202001

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Pancuronium (NAP) - PSUSA/00002275/201912

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

¹⁵ Antihemophilic factor A

¹⁶ Nationally approved product(s) only

¹⁷ Parenteral preparation(s) only, except iron dextran

Action: For adoption of recommendation to CMDh

6.3.17. Sodium fluoride (¹⁸F) (NAP) - PSUSA/00010706/201911

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Sulbactam (NAP) - PSUSA/00002800/201911

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Tibolone (NAP) - PSUSA/00002947/201912

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Levetiracetam - KEPRA (CAP) - EMEA/H/C/000277/LEG 088.2

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to LEG 088 [cumulative review of cases of cardiac arrhythmia and cases of torsades de pointes/QT prolongation as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001846/201811) adopted in July 2019] as per the request for supplementary information (RSI) adopted in May 2020

Action: For adoption of advice to CHMP

6.4.2. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/LEG 015

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Martin Huber

Scope: Details on study Truven MarketScan¹⁸ and cumulative review of cases of intestinal perforation as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010025/201908) adopted in March 2020

¹⁸ Truven MarketScan claims database used to assess the potential association between linaclotide and gastrointestinal (GI) perforation

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

None

6.6. Expedited summary safety reviews¹⁹

6.6.1. Remdesivir – VEKLURY (compassionate use²⁰) - EMEA/H/K/5622/CU/PSM 002

Applicant: Gilead Sciences Ireland UC

Scope: Second expedited summary safety report for remdesivir covering the period from 06 May 2020 to 04 June 2020 as a condition for the safety monitoring in frame of the compassionate use for remdesivir, indicated in a compassionate use programme for the treatment of adults with coronavirus disease 2019 (COVID-19) who require invasive mechanical ventilation

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. Aprotinin (NAP) - EMEA/H/N/PSA/J/0046.1

Applicant: Nordic Group BV (Trasylol) (on behalf of a consortium)

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to PSA/J/0046 [substantial amendment to a previously agreed protocol (N/PSP/0004.1) in March 2015 for a joint non-interventional study: Nordic aprotinin patient registry to record utilisation information on patients at cardiac surgery centres] 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. Sotagliflozin – ZYNQUISTA (CAP) - EMEA/H/C/PSP/S/0084.2

Applicant: Navigant Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0084.1 [protocol for an observational retrospective cohort study using existing data sources on the incidence of diabetic ketoacidosis (DKA) in adult patients with type 1 diabetes mellitus (T1DM) treated with sotagliflozin as an adjunct to insulin versus insulin alone, as required in the outcome of the initial opinion/marketing authorisation (EMEA/H/C/004889) finalised in February 2019] as per the request for supplementary information (RSI) adopted in February 2020

¹⁹ Requirement to the compassionate use opinion to submit expedited summary safety reports for review accompanied by a summary of remdesivir distribution, In addition to the 6-monthly or annual PSURs falling within the pandemic period

²⁰ CHMP opinion on the compassionate use in accordance with Article 83(3) of Regulation (EC) No 726/2004 adopted on 02 April 2020

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

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

7.1.3. Valproate²² (NAP) - EMEA/H/N/PSP/J/0074.3

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

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to PSP/J/0074.2 [protocol for a joint observational study to evaluate and identify the best practices for switching of valproate in clinical practice, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in March 2020

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

7.1.4. Volanesorsen – WAYLIVRA (CAP) - EMEA/H/C/PSP/S/0080.3

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0080.2 [protocol for study WAY4001: a multinational observational registry of patients treated with volanesorsen to evaluate the safety on severe thrombocytopenia and bleeding in patients with familial chylomicronemia syndrome (FCS)] as per the request for supplementary information (RSI) adopted in April 2020

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)²³

7.2.1. Fostamatinib - TAVLESSE (CAP) - EMEA/H/C/005012/MEA 002

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study BIG-CL-PRT-000015: a post-authorisation long term safety surveillance study of fostamatinib in adult patients with chronic immune thrombocytopenia (cITP) who are refractory to other treatments (from initial opinion/marketing authorisation(s) (MA)) [final clinical study report (CSR) expected in March 2025]

Action: For adoption of advice to CHMP

7.2.2. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/MEA 006

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Protocol for study ALN-AS1-006: a global observational longitudinal prospective registry of patients with acute hepatic porphyria (AHP) [ELEVATE]

Action: For adoption of advice to CHMP

²² Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium

²³ 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

7.2.3. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/MEA 014.3

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 014.2 [protocol for study E7080-G000-508: an observational study to characterise hepatic related toxicity and overall safety profile in real-life conditions in the EU (Western population) in hepatocellular carcinoma (HCC) patients, including patients with Child-Pugh B] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.2.4. Loxapine - ADASUVE (CAP) - EMEA/H/C/002400/MEA 001.5

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Substantial amendment to a protocol previously agreed in May 2018 for study AMDC-204-401: a post-authorisation observational study to evaluate the safety of Adasuve (loxapine for inhalation) in agitated persons in routine clinical care and study

Action: For adoption of advice to CHMP

7.2.5. Lutetium (¹⁷⁷Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.4

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 001.3 [first progress report for study A-LUT-T-E02-402 (SALUS study) (listed as a category 3 study in the RMP): an international post-authorisation safety registry to assess the long-term safety of Lutathera (lutetium (¹⁷⁷Lu)) for unresectable or metastatic, somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs) [final clinical study report (CSR) expected in December 2025]] as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.2.6. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 002.6

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Substantial amendment to a protocol previously agreed in November 2015 for study D3820R00006: a post-marketing observational drug utilisation study (DUS) of Moventig (naloxegol) conducted in selected European populations in order to describe demographic, clinical, and treatment characteristics in the baseline of patients treated with naloxegol as well as to describe treatment pattern characteristics of naloxegol utilisation at initiation and follow-up

Action: For adoption of advice to CHMP

7.2.7. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 002.4

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 002 [the safety of Onpattro (patisiran) in a real-world cohort of hereditary transthyretin amyloidosis (hATTR) patients] as per the request for supplementary information (RSI) adopted in April 2020

Action: For adoption of advice to CHMP

7.2.8. Solriamfetol - SUNOSI (CAP) - EMEA/H/C/004893/MEA 002

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Protocol for study JZP865-401: a PASS to evaluate the long-term safety of solriamfetol in adult patients with obstructive sleep apnoea (OSA) treated with solriamfetol (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CHMP

7.2.9. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/MEA 041.6

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Substantial amendment to a protocol previously agreed in November 2018 for study WA29358: an observational safety and effectiveness study of patients with polyarticular juvenile idiopathic arthritis treated with tocilizumab

Action: For adoption of advice to CHMP

7.2.10. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 014

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study A3921321: a drug utilisation study (DUS) on the utilisation and prescribing patterns of xeljanz (tofacitinib) in two European countries using administrative claims databases and national registries for assessment, as requested in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMA/H/A-20/1485) finalised in November 2019

Action: For adoption of advice to CHMP

7.2.11. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 015

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 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 (EMA/H/A-20/1485) finalised in November 2019

Action: For adoption of advice to CHMP

7.2.12. Ustekinumab - STELARA (CAP) - EMA/H/C/000958/MEA 044.8

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Substantial amendment to a protocol previously agreed in October 2019 for study CNT01275PSO4056: an observational PASS of ustekinumab in the treatment of paediatric patients aged 12 years and older with moderate to severe plaque psoriasis (adolescent registry) as requested in the conclusion of variation II/0073 finalised in December 2019

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)²⁴

7.3.1. Iron^{25 26} (NAP) - EMA/H/N/PSR/J/0026

Applicant: Mesama Consulting (on behalf of a consortium) (Cosmofer, Ferinject, Monofer, Venofer)

PRAC Rapporteur: Adrien Inoubli

Scope: Results for a joint study on intravenous iron: evaluation of the risk of severe hypersensitivity reactions, as imposed in the conclusions of the referral under Article 31 of Directive 2001/83/EC (EMA/H/A-31/1322) for intravenous (IV) iron-containing medicines in 2013

Action: For adoption of recommendation to CMDh

7.4. Results of PASS non-imposed in the marketing authorisation(s)²⁷

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

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

²⁵ Intravenous (IV)

²⁶ Iron(III)-hydroxide dextran complex, iron sucrose complex/iron(III)-hydroxide sucrose complex, ferric carboxymaltose complex, iron(III) isomaltoside complex, sodium ferric gluconate complex

²⁷ 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

(version 8.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

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. [Alglucosidase alfa - MYOZYME \(CAP\) - EMEA/H/C/000636/II/0079](#)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final report from study ALGMYC07390: prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions to test the effectiveness of the approved safety information packet (SIP) (in fulfilment of MEA 053)

Action: For adoption of PRAC Assessment Report

7.4.4. [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

7.4.5. [Degarelix - FIRMAGON \(CAP\) - EMEA/H/C/000986/II/0037](#)

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' in order to revise the additional risk minimisation measures (educational programme) based on previous assessment and results from study FE 200486 CS39: a prospective observational safety study in patients with advanced prostate cancer treated with Firmagon (degarelix) or a gonadotropin-releasing hormone (GnRH) agonist conducted in multiple countries in the European Economic Area (EEA). As a consequence, the RMP (version 16.0) is updated accordingly. The MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems', to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1) and to propose a combination of different strengths in the product information

Action: For adoption of PRAC Assessment Report

7.4.6. [Dulaglutide - TRULICITY \(CAP\) - EMEA/H/C/002825/II/0048](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of the final study report from study B010 (listed as a category 3 study in the RMP) investigating the utilisation of dulaglutide in European countries: a cross-sectional, multi-country and multi-source drug utilisation study using electronic health record databases (in fulfilment of MEA 001). The RMP (version 5.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. [Dulaglutide - TRULICITY \(CAP\) - EMEA/H/C/002825/II/0051](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

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

Action: For adoption of PRAC Assessment Report

7.4.8. [Estrogens conjugated, bazedoxifene - DUAVIVE \(CAP\) - EMEA/H/C/002314/II/0025](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report (CSR) for study B2311061 (listed as a category 3 study in the RMP): a non-interventional EU drug utilisation study (DUS) to describe baseline characteristics and utilisation patterns of EU patients initiating Duavive (estrogens conjugated/bazedoxifene) or oestrogen + progestin (E+P) combination hormone

replacement therapy (HRT) (in fulfilment of MEA 003)

Action: For adoption of PRAC Assessment Report

7.4.9. Fampridine - FAMPYRA (CAP) - EMEA/H/C/002097/II/0046

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.2, 4.3, 4.4, 4.8, 4.9 and 5.2 of the SmPC in order to remove the contraindication for patients with mild renal impairment, add a warning for patients with mild renal impairment, update the frequency of seizure to 'uncommon', add vertigo with frequency common, add dizziness in section 4.9 to reflect safety information based on the final results of study 218MS401 (LIBERATE) (listed as category 3 study in the RMP): a phase 4 prospective, non-interventional, multicentre, observational study in multiple sclerosis (MS) patients who began Fampyra (fampridine) treatment in the post-marketing setting. The package leaflet is updated accordingly. The RMP (version 13.1) is also updated accordingly and in line with revision 2.0 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

7.4.10. Hydroxycarbamide - SIKLOS (CAP) - EMEA/H/C/000689/II/0045

Applicant: Addmedica S.A.S.

PRAC Rapporteur: Laurence de Fays

Scope: Update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.8 and 4.9 of the SmPC in order to reflect the final study results of non-interventional cohort study ESCORT-HU (European Sickle Cell Disease Cohort-Hydroxyurea): an observational prospective cohort study to measure the occurrence of adverse events and serious adverse events and to harmonise the product information with other hydroxyurea (HU)-containing products. In addition, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is amended to delete the reference to the treatment guide for physicians. The package leaflet and the RMP (version 20) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.11. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/II/0113

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study 20160176 (listed as a category 3 study in the RMP): a retrospective cohort study with the time from index date to diagnosis of myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML) as a primary outcome

Action: For adoption of PRAC Assessment Report

7.4.12. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0085

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the results of study RFB002F2401 (OBTAIN): a 36-month observational study to describe the long-term efficacy and safety of ranibizumab 0.5 mg treatment, in patients with visual impairment due to choroidal neovascularisation (CNV) secondary to pathologic myopia (PM)

Action: For adoption of PRAC Assessment Report

7.4.13. [Rasagiline - AZILECT \(CAP\) - EMEA/H/C/000574/WS1749/0084; RASAGILINE RATIOPHARM \(CAP\) - EMEA/H/C/003957/WS1749/0016](#)

Applicant: Teva B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study TV1030-CNS-50024 (listed as a category 3 study in the RMP): a non-interventional retrospective cohort study which was conducted using the United States Medicare research database to assess the potential risk of melanoma associated with the use of rasagiline mesylate in patients with Parkinson's disease

Action: For adoption of PRAC Assessment Report

7.4.14. [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): registry to estimate the incidence of osteosarcoma in patients who have received treatment with Forteo (teriparatide)

Action: For adoption of PRAC Assessment Report

7.4.15. [Umeclidinium - INCRUSE ELLIPTA \(CAP\) - EMEA/H/C/002809/WS1761/0028; ROLUFTA ELLIPTA \(CAP\) - EMEA/H/C/004654/WS1761/0013; umeclidinium, vilanterol - ANORO ELLIPTA \(CAP\) - EMEA/H/C/002751/WS1761/0029; LAVENTAIR ELLIPTA \(CAP\) - EMEA/H/C/003754/WS1761/0032](#)

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of the final report from study WWE117397 (listed as a category 3 study in the RMP): a retrospective longitudinal non-interventional observational study of new users of inhaled umeclidinium/vilanterol (UMEC/VI) or new users of inhaled umeclidinium (UMEC) or new users of long-acting bronchodilators (LABD) in the primary care setting

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. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/ANX 005.5

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Sixth annual report (reporting period: 14 February 2019 to 13 February 2020) for the multicentre, multinational, observational Morquio A registry study (MARS): a voluntary observational registry study to characterise and describe the mucopolysaccharidosis IV type A (MPS IVA) population and to evaluate the long-term effectiveness and safety of Vimizim (elosulfase alfa) [final clinical study report (CSR) expected by March 2025]

Action: For adoption of advice to CHMP

7.5.2. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 002.2

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a prospective study (listed as a category 3 study in the RMP) to treat patients with rheumatological disorders with biological agents to assess long-term toxicity of these agents in routine clinical practice using the British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA): an established nationwide register [final clinical study report (CSR) expected in 2027]

Action: For adoption of advice to CHMP

7.5.3. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 003

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a study (listed as a category 3 study in the RMP): a national prospective, observational, uncontrolled cohort study whose objectives are to evaluate the risk of selected adverse events (AEs) in rheumatoid arthritis (RA), juvenile idiopathic arthritis, and other rheumatic disease patients treated with infliximab using the Anti-Rheumatic Therapies in Sweden (ARTIS) national surveillance programme [final clinical study report (CSR) expected in 2027]

Action: For adoption of advice to CHMP

7.5.4. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 005.2

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a study (listed as a category 3 study in the RMP): a prospective, observational cohort study whose objectives are to evaluate the long-term effectiveness, safety, and costs associated with tumour necrosis factor (TNF)-inhibitor therapies in the treatment of rheumatoid arthritis (RA) and to compare this to a cohort of

RA patients who are treated with non-biologic disease-modifying antirheumatic drugs (DMARDs) using the German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) [final clinical study report (CSR) expected in 2027]

Action: For adoption of advice to CHMP

7.5.5. [Infliximab - FLIXABI \(CAP\) - EMEA/H/C/004020/MEA 006.2](#)

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a study (listed as a category 3 in the RMP) conducted in the Spanish register of adverse events of biological therapies in rheumatic diseases (BIOBADASER) to identify relevant adverse events occurring during treatment of rheumatic diseases with biological therapies, to estimate the frequency of their occurrence; to identify unexpected adverse events; to identify relevant adverse events that occur following the suspension of the treatment, to estimate the relative risk of occurrence of adverse events with biological therapies in patients with rheumatoid arthritis (RA) compared to those not exposed to these treatments; to identify risk factors for suffering adverse reactions with these treatments; to evaluate, under non-experimental conditions, the treatment duration before the biological medications had been suspended in patients with rheumatic diseases, as well as the reasons for the interruption of the treatment [final clinical study report (CSR) expected in 2027]

Action: For adoption of advice to CHMP

7.5.6. [Influenza vaccine \(live attenuated, nasal\) - FLUENZ TETRA \(CAP\) - EMEA/H/C/002617/MEA 004.11](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual interim report for the passive enhanced safety surveillance study (ESS) D2560C00008: a postmarketing non-interventional cohort study of the safety of live attenuated influenza vaccine (LAIV) in subjects 2 through 17 years of age for the 2019-2020 influenza season in England

Action: For adoption of advice to CHMP

7.5.7. [Octocog alfa - KOVALTRY \(CAP\) - EMEA/H/C/003825/MEA 005.2](#)

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual interim results 2019 for epidemiological study 15689: an evaluation of adverse events of special interest (AESI) in the PEDiatric NETwork (PedNet) haemophilia registry

Action: For adoption of advice to CHMP

7.5.8. [Vedolizumab - ENTYVIO \(CAP\) - EMEA/H/C/002782/MEA 001](#)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: 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] (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Avatrombopag - DOPTelet (CAP) - EMEA/H/C/004722/MEA 002.1

Applicant: Dova Pharmaceuticals Ireland Limited

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002 [feasibility assessment for study AVA-CLD-402: evaluation of the feasibility of conducting a PASS of Doptelet (avatrombopag) in patients with severe chronic liver disease (CLD) and potential utilisation of data from TARGET PharmaSolutions' ongoing observational studies in patients with severe CLD] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.6.2. Evolocumab - REPATHA (CAP) - EMEA/H/C/003766/MEA 009.2

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: MAH's response to MEA 009.1 [feasibility/futility report for study 20150162 (listed as a category 3 study in the RMP) with a protocol previously agreed in March 2016: a multi-national observational study to evaluate the safety of Repatha (evolocumab) in pregnancy [final report expected in Q2 2027]] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

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

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. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - EMEA/H/C/004061/S/0014 (without RMP)

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/S/0087 (without RMP)

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/R/0079 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/R/0021 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Recombinant vesicular stomatitis virus-Zaire ebolavirus vaccine (live) - ERVEBO (CAP) - EMEA/H/C/004554/R/0004 (without RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Aripiprazole - ARIPIRAZOLE ACCORD (CAP) - EMEA/H/C/004021/R/0019 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Birch bark extract - EPISALVAN (CAP) - EMEA/H/C/003938/R/0018 (without RMP)

Applicant: Amryt GmbH

PRAC Rapporteur: Zane Neikena

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Brivaracetam - BRIVIACT (CAP) - EMEA/H/C/003898/R/0025 (with RMP)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Cabazitaxel - JEVTANA (CAP) - EMEA/H/C/002018/R/0042 (with RMP)

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Cinacalcet - CINACALCET MYLAN (CAP) - EMEA/H/C/004014/R/0011 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and haemophilus type b conjugate vaccine (adsorbed) - VAXELIS (CAP) - EMEA/H/C/003982/R/0065 (with RMP)

Applicant: MCM Vaccine B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. [Elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide - GENVOYA \(CAP\) - EMEA/H/C/004042/R/0069 \(with RMP\)](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. [Eptifibatide - EPTIFIBATIDE ACCORD \(CAP\) - EMEA/H/C/004104/R/0010 \(without RMP\)](#)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. [Lopinavir, ritonavir – LOPINAVIR/RITONAVIR MYLAN \(CAP\) - EMEA/H/C/004025/R/0014 \(without RMP\)](#)

Applicant: Mylan S.A.S

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. [Lumacaftor, ivacaftor - ORKAMBI \(CAP\) - EMEA/H/C/003954/R/0056 \(with RMP\)](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. [Octocog alfa - KOVALTRY \(CAP\) - EMEA/H/C/003825/R/0030 \(without RMP\)](#)

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Pemetrexed - PEMETREXED ACCORD (CAP) - EMEA/H/C/004072/R/0012 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Rasagiline - RASAGILINE MYLAN (CAP) - EMEA/H/C/004064/R/0006 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.14. Sufentanil - ZALVISO (CAP) - EMEA/H/C/002784/R/0016 (without RMP)

Applicant: Grunenthal GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/II/0052; dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/II/0001; dolutegravir, lamivudine,

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: PRAC consultation on variations consisting of an update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the dolutegravir (DTG)-containing regimens based on interim analysis from Tsepamo study: a birth outcomes surveillance study being conducted in Botswana designed to evaluate adverse birth outcomes by human immunodeficiency virus (HIV) status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegravir

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Amoxicillin (NAP); amoxicillin, clavulanic acid (NAP) - NL/H/xxxx/WS/371

Applicant(s): Astellas Pharma Europe B.V. (Flemoxin (amoxicillin trihydrate), Forcid Solutab (amoxicillin/clavulanic acid))

PRAC Lead: Liana Gross-Martirosyan

Scope: PRAC consultation on the evaluation of a national variation proposing to add acute pancreatitis as an adverse drug reaction (ADR) with a frequency 'not known', on request of the Netherlands

Action: For adoption of advice to Member States

11.1.2. Retinoids²⁸: acitretin (NAP), alitretinoin (NAP), isotretinoin (NAP) - DE/H/xxxx/WS/627

Applicant(s): Puren Pharma GmbH & Co. KG. (Acicutan (acitretin), Aknenormin (isotretinoin), Isoderm (isotretinoin), IsoGalen (isotretinoin), Isotret-Hexal (isotretinoin), Isotretinoin Basics (isotretinoin), Isotretinoin Puren (isotretinoin), Isotretinoin-ratiopharm (isotretinoin), Neotigason (acitretin), Toctino (alitretinoin))

PRAC Lead: Martin Huber

Scope: PRAC consultation on the evaluation of a national worksharing variation assessing a protocol for a category 3 study: a patient and prescriber survey: effectiveness measures to investigate awareness, knowledge and adherence to the risk minimisation measures (RMMs) of the pregnancy prevention programme (PPP) for oral retinoids (acitretin, alitretinoin, and isotretinoin), on request of Germany

Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Chlormadinone acetate, ethinylestradiol (NAP)

Applicant: Gedeon Richter Plc

PRAC Lead: Martin Huber

Scope: PRAC consultation on the evaluation of interim results for non-interventional imposed study RIVET-CC: a case control study comparing levonorgestrel and chlormadinone acetate in order to evaluate the role of oral contraceptives and the Risk of Venous Thromboembolism (VTE), as imposed in the conclusions of referral procedure under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1356) for combined hormonal contraceptives finalised in 2013), on request of Germany

Action: For adoption of advice to Member States

11.2.2. Lenalidomide (pre-authorisation) - IS/H/0376-0388, 0413-0416/001-007/DC

Scope: PRAC consultation on the evaluation of an initial marketing authorisation application under the decentralised procedure for a generic lenalidomide-containing medicinal product in order to consider the need for additional pharmacovigilance activities and risk minimisation measures, on request of Iceland

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals -Q2 2020

Action: For discussion

²⁸ Oral presentations

- 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. Pharmaceutical strategy for Europe

- 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. Marketing authorisation applications (MAA) forecast for 2020 – planning update dated Q2 2020

- Action: For discussion
- 12.8.2. PRAC workload statistics – Q2 2020

- Action: For discussion
- 12.9. Pharmacovigilance audits and inspections
- 12.9.1. Pharmacovigilance systems and their quality systems

- None
- 12.9.2. Pharmacovigilance inspections

- None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.10.5. Periodic safety update reports single assessment (PSUSA) – Joint PRAC/CMDh action group on 'other consideration' section -update to the assessment report template

PRAC lead: Martin Huber, Menno van der Elst, Jana Lukacisinova, Michal Radik

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 – status of lenalidomide-containing product(s)

PRAC lead: Eva Segovia, Maria del Pilar Rayon

Action: For adoption

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.14.3. Good pharmacovigilance practice (GVP) module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' – revision 3

PRAC lead: Sabine Straus

Action: For adoption

12.14.4. Initial marketing authorisation applications (MAA) – review of PRAC rapporteur assessment report templates for RMP (D-94) - revision

Action: For discussion

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

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

PRAC lead: Menno van der Elst, Martin Huber

Action: For adoption

12.20.2. Rapid data analytical process - Interim results

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/