03 February 2023
EMA/PRAC/12766/2023 Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 06-09 February 2023

Chair: Sabine Straus – Vice-Chair: Martin Huber

06 February 2023, 13:00 – 19:30, room 1C / via teleconference

07 February 2023, 08:30 – 19:30, room 1C / via teleconference

08 February 2023, 08:30 – 19:30, room 1C / via teleconference

09 February 2023, 08:30 – 16:00, room 1C / via teleconference

Organisational, regulatory and methodological matters (ORGAM)

23 February 2023, 09:00 - 12:00, via teleconference

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

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

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

Note on access to documents

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

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

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 February 2023. See February 2023 PRAC minutes (to be published post March 2023 PRAC meeting).

1.2. Agenda of the meeting on 06-09 February 2023

Action: For adoption

1.3. Minutes of the previous meeting on 09-12 January 2023

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

3.1.1. Pseudoephedrine (NAP); pseudoephedrine, acetylsalicylic acid (NAP); pseudoephedrine, acetylcysteine, paracetamol (NAP); pseudoephedrine, acrivastine (NAP); pseudoephedrine, ascorbic acid, paracetamol (NAP); pseudoephedrine, cetirizine (NAP); pseudoephedrine, ebastine (NAP); pseudoephedrine, guaifenesin (NAP); pseudoephedrine, ibuprofen (NAP); pseudoephedrine, chlorphenamine (NAP); pseudoephedrine, chlorphenamine, codeine (NAP); pseudoephedrine, chlorphenamine, dextromethorphan (NAP); pseudoephedrine, chlorphenamine,

paracetamol (NAP); pseudoephedrine, chlorphenamine, dextromethorphan, paracetamol (NAP); pseudoephedrine, dextromethorphan (NAP); pseudoephedrine, dextromethorphan, paracetamol (NAP); pseudoephedrine, dextromethorphan, ascorbic acid, paracetamol (NAP); pseudoephedrine, dextromethorphan, guaifenesin, paracetamol (NAP); pseudoephedrine, dextromethorphan, guaifenesin, triprolidine (NAP); pseudoephedrine, dextromethorphan, triprolidine (NAP); pseudoephedrine, diphenhydramine, paracetamol (NAP); pseudoephedrine, doxylamine, paracetamol (NAP); pseudoephedrine, loratadine (NAP); pseudoephedrine, paracetamol (NAP); pseudoephedrine, paracetamol, pholcodine (NAP); pseudoephedrine, triprolidine (NAP); pseudoephedrine, triprolidine, guaifenesin (NAP); pseudoephedrine, triprolidine, paracetamol (NAP); pseudoephedrine, desloratadine - aerinaze (CAP) – EMA/H/A31/1526

Applicant(s): various

PRAC Rapporteur: To be appointed; PRAC Co-rapporteur: To be appointed

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

Action: For adoption of a list of questions

3.2. Ongoing procedures

3.2.1. Topiramate (NAP); topiramate, phentermine (NAP) - EMEA/H/A-31/1520

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Martin Huber

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

Action: For agreement on the list of participants (LoP) for a scientific advisory group (SAG) meeting

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

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

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Ipilimumab – YERVOY (CAP); nivolumab – OPDIVO (CAP); pembrolizumab – KEYTRUDA (CAP)

Applicant(s): Bristol-Myers Squibb Pharma EEIG (OPDIVO, YERVOY), Merck Sharp & Dohme B.V. (KEYTRUDA)

PRAC Rapporteur: To be appointed

Scope: Signal of capillary leak syndrome (OPDIVO, YERVOY, KEYTRUDA) and cytokine release syndrome (OPDIVO)

Action: For adoption of PRAC recommendation

EPITT 19880 – New signal

Lead Member State(s): NL

4.1.2. Tofacitinib – XELJANZ (CAP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of acnes

Action: For adoption of PRAC recommendation

EPITT 19885 – New signal

Lead Member State(s): NL

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Adalimumab - AMGEVITA (CAP), AMSPARITY (CAP), HEFIYA (CAP), HUMIRA (CAP) - EMEA/H/C/000481/SDA 126, HULIO (CAP), HUKYNDRA (CAP), HYRIMOZ (CAP), IDACIO (CAP), IMRALDI (CAP), LIBMYRIS (CAP), YUFLYMA (CAP); etanercept – ENBREL (CAP) – EMEA/H/C/000262/SDA 175; infliximab – REMICADE (CAP) – EMEA/H/C/000240/SDA 162

Applicant(s): AbbVie Deutschland GmbH (Humira), Amgen Europe B.V.(Amgevita), Celltrion Healthcare Hungary Kft. (Yuflyma), Fresenius Kabi Deutschland GmbH (Idacio), Janssen Biologics B.V. (Remicade),

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

Pfizer Europe MA EEIG (Amsparity, Enbrel), Sandoz GmbH (Hyrimoz, Hefiya), Samsung Bioepis NL B.V. (Imraldi), Stada Arzneimittel AG (Hukyndra, Libmyris), Viatris Limited (Hulio),

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of menstrual disorder

Action: For adoption of PRAC recommendation

EPITT 19812 – Follow-up to June 2022

4.3.2. Bosutinib – BOSULIF (CAP) – EMEA/H/C/002373/SDA 016

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Signal of interstitial lung disease (ILD)

Action: For adoption of PRAC recommendation

EPITT 19843 – Follow-up to October 2022

4.3.3. Colistimethate sodium[3] (NAP)

Applicant(s): various

PRAC Rapporteur: Adam Przybylkowski

Scope: Signal of pseudo-bartter syndrome

Action: For adoption of PRAC recommendation

EPITT 19845 – Follow-up to October 2022

4.3.4. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/SDA 049

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

Scope: Signal of morphoea

Action: For adoption of PRAC recommendation

EPITT 19839 – Follow-up to October 2022

4.4. Variation procedure(s) resulting from signal evaluation

None

[3] For intravenous use only

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Adagrasib - EMEA/H/C/006013

Scope : Treatment of patients with advanced non-small cell lung cancer (NSCLC) with KRAS G12C mutation

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

5.1.2. Dabigatran etexilate - EMEA/H/C/005922

Scope : Prevention of venous thromboembolic events

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

5.1.3. Eculizumab - EMEA/H/C/006036

Scope : Treatment of paroxysmal nocturnal haemoglobinuria

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

5.1.4. Enalapril maleate - EMEA/H/C/005731, PUMA[4]

Scope : Treatment of heart failure

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

5.1.5. Futibatinib - EMEA/H/C/005627, Orphan

Applicant: Taiho Pharma Netherlands B.V.

Scope : Treatment of cholangiocarcinoma

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

5.1.6. Glofitamab - EMEA/H/C/005751, Orphan

Applicant: Roche Registration GmbH

Scope : Treatment of diffuse large B-cell lymphoma

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

5.1.7. Ivosidenib - - EMEA/H/C/005936, Orphan

Applicant: Les Laboratoires Servier

[4] Paediatric-use marketing authorisation(s)

Scope : Treatment of acute myeloid leukaemia and treatment of metastatic cholangiocarcinoma

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

5.1.8. Ivosidenib - EMEA/H/C/006174, Orphan

Applicant: Les Laboratoires Servier

Scope : Treatment of acute myeloid leukaemia

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

5.1.9. Lacosamide - EMEA/H/C/006047

Scope : Treatment of epilepsy

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

5.1.10. Pirtobrutinib - EMEA/H/C/005863, Orphan

Applicant: Eli Lilly Nederland B.V.

Scope : Treatment of mantle cell lymphoma (MCL)

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

5.1.11. Sugammadex - EMEA/H/C/006046

Scope : Reversal of neuromuscular blockade induced by rocuronium or vecuronium

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

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

5.2.1. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - EMEA/H/C/005737/II/0065

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP version 5.1 in order to update the clinical exposure and risk sections

Action: For adoption of PRAC Assessment Report

5.2.2. Micafungin - MYCAMINE (CAP) - EMEA/H/C/000734/II/0047

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of Annex II and the RMP to version 23.0 to include the results of the non-interventional

PASS 9463-PV-0002: effectiveness check of the prescriber checklist for Mycamine (micafungin)

Action: For adoption of PRAC Assessment Report

5.2.3. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/II/0061

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 12 in order to remove certain risks from the list of safety concerns

Action: For adoption of PRAC Assessment Report

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

5.3.1. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0074

Applicant: Roche Registration GmbH

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Submission of the final report from study MO39171 listed as a category 3 study in the RMP in order to fulfil MEA/008. This is a Phase III/IV, Single Arm, multicentre, interventional study of Atezolizumab to Investigate Long-term Safety and Efficacy in previously treated Patients with Locally Advanced or Metastatic Non-small Cell Lung Cancer (NSCLC). The RMP version 23 has also been submitted

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

5.3.2. Atidarsagene autotemcel - LIBMELDY (CAP) - EMEA/H/C/005321/II/0011/G, Orphan

Applicant: Orchard Therapeutics (Netherlands) B.V., ATMP[5]

PRAC Rapporteur: Gabriele Maurer

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.4, 4.5, 4.8, and 5.1 of the SmPC in order to remove the option of using bone marrow (BM) as a cellular source for the manufacture of Libmeldy, as a result of an evolution of clinical practices and also to rationalise the manufacture of this highly complex medicinal product; the package leaflet and labelling are updated accordingly. In addition, the MAH took the opportunity to remove ANX/002 from the Annex II and to introduce minor editorial changes to the product information. The RMP version 1.3 has also been submitted; 2) other quality related variations

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

5.3.3. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/II/0022, Orphan

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

[5] Advanced therapy medicinal product

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations and to update pharmacokinetic information for use in patients with severe hepatic impairment based on the final results from study BLU-285-0107 listed as a category 3 study in the RMP; this is a phase 1, open-label, single-dose study to investigate the influence of severe hepatic impairment on the pharmacokinetics of avapritinib. The package leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template version 10.3

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

5.3.4. Casirivimab, imdevimab - RONAPREVE (CAP) - EMEA/H/C/005814/II/0002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of coronavirus (COVID-19) in hospitalised patients in adults and adolescents aged 12 years and older weighing at least 40 kg. As a consequence, sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The package leaflet, the labelling and the RMP (version 1.1) are updated in accordance

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

5.3.5. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0084/G

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of an updated RMP version 6.1 in order to request the discontinuation of the category 1 study D8111C00010 and remove it from the Annex II; this is an interventional safety study of AZD1222 vaccine in immunocompromised adults. In addition, the MAH proposes the reassessment of safety concerns and changes to due dates of additional pharmacovigilance activities

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

5.3.6. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - EMEA/H/C/002246/II/0057, Orphan

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Submission of the 24-months' CSR addendum of the MW2010-03-02 (DETECT) category 1 study; a multicentre, multinational, randomised, controlled, assessor blinded study, performed in subjects with thermal burns, to evaluate the efficacy and safety of NexoBrid compared to gel vehicle and compared to standard of care. The provision of the CSR addresses the post-authorisation measure ANX 001.7. An updated RMP version 8.0 was provided as part of the application

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

5.3.7. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0126, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Monica Martinez Redondo

Scope: Extension of indication to include treatment of paediatric patients with refractory generalised myasthenia gravis (gMG) for Soliris, based on interim results from study ECU-MG-303; this is an open-label, multicentre, phase 3 study to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of intravenous (IV) eculizumab in paediatric patients aged 6 to less than 18 years with acetylcholine receptor-antibody (AChR-Ab) positive (+) refractory gMG. 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 is updated in accordance. Version 20.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to update section 4.8 of the SmPC in order to update the frequency of the list of adverse drug reactions (ADRs) based on cumulative safety data and to introduce minor editorial changes to the product information

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

5.3.8. Faricimab - VABYSMO (CAP) - EMEA/H/C/005642/II/0002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information and to update the warnings and the list of adverse drug reactions (ADRs), based on longer-term results from studies GR40306 (TENAYA) and GR40844 (LUCERNE); these are phase 3, multicentre, randomised, double-masked, active comparator-controlled, 112-week studies to evaluate the efficacy and safety of faricimab in patients with neovascular age-related macular degeneration (nAMD); the package leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, 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. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0013/G, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final reports from studies ALN-AS1-003 (Study 003) and ALN-AS1-002 (Study 002) listed as a category 3 studies in the RMP. Study 003 is a phase 3 randomised, double-blind, placebo-controlled multicentre study with an open-label extension to evaluate the efficacy and safety of givosiran in patients with acute hepatic porphyrias, while Study 002 is a multicentre, open-label extension study to evaluate the long-term safety and clinical activity of subcutaneously administered ALN AS1 in patients with acute intermittent porphyria who have completed a previous clinical study with ALN-AS1. The RMP version 2.2 has also been submitted

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

5.3.10. Granisetron - SANCUSO (CAP) - EMEA/H/C/002296/II/0061

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Update of sections 4.4, 4.6, 4.7, 4.8, 4.10 and 5.3 of the SmPC in order to add 'Serotonin syndrome' and 'Application site Reactions' to the list of adverse drug reactions (ADRs) with frequency 'unknown'; as well as 'Application site Irritation' with frequency 'uncommon' based on post-marketing data and literature. The MAH also proposes to update sections 4.4 and 4.5 of the SmPC to add drug-drug interaction information with buprenorphine/opioids and serotonergic medicinal products based on post-marketing data and literature. The package leaflet has been updated accordingly. The RMP version 5 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes in the SmPC.

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

5.3.11. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0123

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 4.4 of the SmPC, Annex IID and Article 127a and the tools/documents included in the Educational Healthcare Professional Kit, in order to harmonise the terminology utilised in the RMP and product information documents relating to the safety concern of teratogenicity and its risk minimisation measure of the Pregnancy Prevention Plan (PPP) across the 3 immunomodulatory imide drugs (IMiDs). These proposed changes will only have a limited impact on the National Competent Authority (NCA)-approved content/text of the educational materials, and the key messages to the HCP and patients. Furthermore, the regulatory obligations regarding the PPP will not be impacted. The MAH is also taking the opportunity to update the RMP with PASS Protocol milestones. The updated RMP version 38 was provided

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

5.3.12. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/II/0052

Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: Update of section 4.8 of the SmPC based on pooled safety data including results of Study 307, an ongoing, multicentre, randomised, open-label study that is being conducted to compare the efficacy and safety of lenvatinib in combination with everolimus or pembrolizumab versus sunitinib as first-line (1L) treatment in adults with advanced renal cell carcinoma (RCC). The provision of the clinical study report (CSR) addresses the post-authorisation measure MEA/FSR 009.3. The package leaflet is updated accordingly. An updated RMP version 15.0 has been submitted

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

5.3.13. Lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/004731/II/0005

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP[6]

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of adult patients with Second-line (2L) Transplant

[6] Advanced therapy medicinal product

Intended (TI) Large B-Cell Lymphoma (LBCL) for BREYANZI, based on interim analyses from pivotal study JCAR017-BCM-003: a global randomised multicentre phase III trial to compare the efficacy and safety of JCAR017 to standard of care in adult subjects with high-risk, transplant-eligible relapsed or refractory aggressive B-cell Non-Hodgkin Lymphomas (TRANSFORM). As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted

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

5.3.14. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/X/0078/G

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped application consisting of: 1) Extension application to add a new strength of 75 mg of lumacaftor and 94 mg of ivacaftor fixed dose combination granules; 2) Extension of indication to include treatment of cystic fibrosis for children aged 1 to less than 2 years old of age who are homozygous for the F508del mutation in the CFTR gene, based on final results from study 122, a 2-part study of cystic fibrosis (CF) subjects 1 to <2 years of age homozygous for F508del. As a consequence, sections 4.1, 4.2, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 11.2 of the RMP has also been submitted

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

5.3.15. Methotrexate - NORDIMET (CAP) - EMEA/H/C/003983/II/0027

Applicant: Nordic Group B.V.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of moderate to severe recalcitrant disabling psoriasis for Nordimet, based on literature. As a consequence, sections 4.1 and 4.2 of the SmPC are updated. The package leaflet is updated in accordance. The RMP (version 6.0) of the RMP has also been submitted

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

5.3.16. Oritavancin - TENKASI (CAP) - EMEA/H/C/003785/X/0036

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to add a new strength of 1200 mg for powder for concentrate for solution for infusion. The RMP (version 4) is updated accordingly

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

5.3.17. Pomalidomide - IMNOVID (CAP) - EMEA/H/C/002682/II/0047, Orphan

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Update of section 4.4 of the SmPC, Annex IID and Article 127a and the tools/documents included

in the Educational Healthcare Professional Kit, in order to harmonise the terminology utilised in the RMP and product information documents relating to the safety concern of teratogenicity and its risk minimisation measure of the Pregnancy Prevention Plan across the 3 immunomodulatory imide drugs (IMiDs). These proposed changes will only have a limited impact on the National Competent Authority (NCA)-approved content/text of the educational materials, and the key messages to the HCP and patients. Furthermore, the regulatory obligations regarding the pregnancy prevention plan (PPP) will not be impacted. The updated RMP version 16 was provided

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

5.3.18. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/II/0010

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy and safety information in the treatment of adult patients with RET fusion-positive advanced non-small cell lung cancer (NSCLC) based on final results (NSCLC indication) from study ARROW/BO42863, a Phase 1/2 Study of the Highly-selective RET Inhibitor, BLU 667, in Patients With Thyroid Cancer, Non-Small Cell Lung Cancer (NSCLC), and Other Advanced Solid Tumours listed as a specific obligation in the Annex II. The RMP version 1.5 has also been submitted

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

5.3.19. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0101

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update information on preterm infants based on final results from study CRFB002H2301E (RAINBOW extension), listed as a PAES in the Annex II; this is an extension study to evaluate the long- term efficacy and safety of ranibizumab compared with laser therapy for the treatment of infants born prematurely with retinopathy of prematurity. The Annex II and package leaflet are updated accordingly. The RMP version 22.0 has also been submitted. In addition, 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

5.3.20. Relugolix, estradiol, norethisterone acetate - RYEQO (CAP) - EMEA/H/C/005267/II/0013/G

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of moderate to severe pain associated with endometriosis for RYEQO in adult women of reproductive age with a history of previous medical or surgical treatment for their endometriosis, based on final results from studies MVT-601-3101 and MVT-601-3102 and final results up to 104 weeks from study MVT-601-3103. Studies 3101 and 3102 are pivotal, phase III, randomised, double-blind, placebo-controlled, safety and efficacy studies to evaluate relugolix with E2 and NETA as a combination therapy for pain associated with endometriosis. Study 3103 is an open-label extension study including patients who completed one of the two pivotal studies and met the

eligibility criteria, regardless of their treatment assignment in the pivotal studies. In the extension part all patients received relugolix combination therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC were updated. The package leaflet is updated in accordance. Update of section 4.5 of the SmPC to update information regarding Drug-Drug Interaction based on final results of DDI studies MVT-601-54, MVT-601-55 and MVT-601-57. Study MVT-601-54 is a 2-part interventional open-label study to assess the potential effects of erythromycin on the PK of the 3 components of Ryeqo. Study MVT-601-55 is an interventional open label fixed single sequence cross-over study to assess whether a 6-hour dose separation is sufficient to mitigate absorption mediated increased exposure to relugolix and study MVT-601-057 is a 2-part study to assess the potential effect of relugolix on the PK of total dabigatran. The updated RMP version (2.0) has also been submitted. As part of the application, the MAH also requests an extension of the market protection by one additional year

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

5.3.21. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0044/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendations for patients with renal impairment, remove an existing warning on renal impairment and update the safety and efficacy information based on final results from studies GS US 540 5912 and GS-US-540-9015, listed as category 3 studies in the RMP. Study GS US 540 5912 is a phase 3 randomised, double-blind, placebo-controlled, parallel group, multicentre study evaluating the efficacy and safety of remdesivir in participants with severely reduced kidney function who were hospitalized for COVID-19, while study GS-US-540-9015 is a phase 1, multicentre, open-label, single-dose study to evaluate the single-dose pharmacokinetic (PK) of remdesivir in participants with normal and impaired renal function. The package leaflet is updated accordingly. The RMP version 5.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor edits to the product information

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

5.3.22. Thalidomide - THALIDOMIDE BMS (CAP) - EMEA/H/C/000823/II/0076

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 4.4 of the SmPC, Annex IID and Article 127a and the tools/documents included in the Educational Healthcare Professional Kit, in order to harmonise the terminology utilised in the RMP and product information documents relating to the safety concern of teratogenicity and its risk minimisation measure of the Pregnancy Prevention Plan (PPP) across the 3 immunomodulatory imide drugs (IMiDs). These proposed changes will only have a limited impact on the National Competent Authority (NCA)-approved content/text of the educational materials, and the key messages to the HCP and patients. Furthermore, the regulatory obligations regarding the PPP will not be impacted. The MAH is also taking the opportunity to update the RMP with PASS Protocol milestones, and to make some editorial changes in the labelling. The updated RMP version 20 was provided

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Aclidinium bromide - BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP) - PSUSA/00009005/202207

Applicant(s): Covis Pharma Europe B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alectinib - ALECENSA (CAP) - PSUSA/00010581/202207

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/202207

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Avapritinib - AYVAKYT (CAP) - PSUSA/00010878/202207

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Beclometasone, formoterol, glycopyrronium bromide - RIARIFY (CAP); TRIMBOW (CAP); TRYDONIS (CAP) - PSUSA/00010617/202207

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

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Belatacept - NULOJIX (CAP) - PSUSA/00000311/202206

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Birch bark extract[7] - FILSUVEZ (CAP) - PSUSA/00010446/202207

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Brexucabtagene autoleucel - TECARTUS (CAP) - PSUSA/00010903/202207

Applicant: Kite Pharma EU B.V. ATMP[8]

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.9. Brinzolamide, brimonidine tartrate - SIMBRINZA (CAP) - PSUSA/00010273/202206

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Budesonide[9] - JORVEZA (CAP) - PSUSA/00010664/202207

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[7] Centrally authorised product(s) only
[8] Advanced therapy medicinal product
[9] Centrally authorised products indicated for eosinophilic esophagitis only

6.1.11. Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/202207

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Casirivimab, imdevimab - RONAPREVE (CAP) - PSUSA/00010963/202207

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Cenegermin - OXERVATE (CAP) - PSUSA/00010624/202207

Applicant: Dompe farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Cladribine[10] - MAVENCLAD (CAP) - PSUSA/00010634/202207

Applicant: Merck Europe B.V.

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Daridorexant - QUVIVIQ (CAP) - PSUSA/00010993/202207

Applicant: Idorsia Pharmaceuticals Deutschland GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Finerenone - KERENDIA (CAP) - PSUSA/00010978/202207

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

[10] For treatment of multiple sclerosis only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Glecaprevir, pibrentasvir - MAVIRET (CAP) - PSUSA/00010620/202207

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Glucagon[11] - BAQSIMI (CAP); OGLUO (CAP) - PSUSA/00010826/202207

Applicant(s): Eli Lilly Nederland B.V. (Baqsimi), Tetris Pharma B.V. (Ogluo)

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Glucarpidase - VORAXAZE (CAP) - PSUSA/00010968/202207

Applicant: SERB S.A.S.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Guselkumab - TREMFYA (CAP) - PSUSA/00010652/202207

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Icosapent ethyl - VAZKEPA (CAP) - PSUSA/00010922/202207

Applicant: Amarin Pharmaceuticals Ireland Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[11] Centrally authorised product(s) only

6.1.22. Imipenem, cilastatin, relebactam - RECARBRIO (CAP) - PSUSA/00010830/202207

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Indacaterol, glycopyrronium, mometasone - ENERZAIR BREEZHALER (CAP); ZIMBUS BREEZHALER (CAP) - PSUSA/00010861/202207

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Inotersen - TEGSEDI (CAP) - PSUSA/00010697/202207

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. L-lysine hydrochloride, l-arginine hydrochloride - LYSAKARE (CAP) - PSUSA/00010786/202207

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Neratinib - NERLYNX (CAP) - PSUSA/00010712/202207

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Odevixibat - BYLVAY (CAP) - PSUSA/00010949/202207

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Perampanel - FYCOMPA (CAP) - PSUSA/00009255/202207

Applicant: Eisai GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Pneumococcal polysaccharide conjugate vaccine (15 valent, adsorbed) - VAXNEUVANCE (CAP) - PSUSA/00010975/202207

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Relugolix - ORGOVYX (CAP) - PSUSA/00010994/202207

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Remimazolam - BYFAVO (CAP) - PSUSA/00010924/202207

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Romosozumab - EVENITY (CAP) - PSUSA/00010824/202207

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Salmeterol, fluticasone propionate[12] - BROPAIR SPIROMAX (CAP); SEFFALAIR SPIROMAX (CAP) - PSUSA/00010928/202207

Applicant(s): Teva B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - PSUSA/00010619/202207

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - PSUSA/00010630/202207

Applicant: Rejuvenate GmbH, ATMP[13]

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.36. Tagraxofusp - ELZONRIS (CAP) - PSUSA/00010896/202207

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/202207

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Centrally authorised product(s) only
[13] Advanced therapy medicinal product

6.1.38. Tecovirimat - TECOVIRIMAT SIGA (CAP) - PSUSA/00010971/202207

Applicant: SIGA Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Vericiguat - VERQUVO (CAP) - PSUSA/00010950/202207

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Voretigene neparvovec - LUXTURNA (CAP) - PSUSA/00010742/202207

Applicant: Novartis Europharm Limited, ATMP[14]

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

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

None

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

6.3.1. Acamporsate (NAP) - PSUSA/00000016/202207

Applicant(s): various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Amorolfine (NAP) - PSUSA/00000185/202206

Applicant(s): various

PRAC Lead: Melinda Palfi

[14] Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Apis mellifera (801), apis mellifera venom[15,16] (NAP) - PSUSA/00010722/202207

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Benserazide, levodopa (NAP) - PSUSA/00000330/202206

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Betula verrucosa[17,18] (NAP) - PSUSA/00010815/202207

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Carbetocin (NAP) - PSUSA/00000546/202206

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Cilastatin, imipenem (NAP) - PSUSA/00000748/202206

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[15] With or without adjuvant
[16] Allergen for diagnostic and/or therapy
[17] Allergen for therapy
[18] Sublingual tablet(s) only

6.3.8. Delapril, manidipine (NAP); delapril, indapamide (NAP) - PSUSA/00010496/202206

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Flecainide (NAP) - PSUSA/00001396/202206

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Ganciclovir (NAP) - PSUSA/00001516/202206

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Glimepiride (NAP) - PSUSA/00001534/202206

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Human coagulation factor XIII (NAP) - PSUSA/00001622/202206

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Hydroquinidine (NAP) - PSUSA/00001688/202207

Applicant(s): various

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Ibuprofen, pseudoephedrine (NAP) - PSUSA/00001711/202207

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Itopride (NAP) - PSUSA/00010606/202206

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Ketotifen[19] (NAP) - PSUSA/00001812/202206

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Methylaminolevulinate (NAP) - PSUSA/00002019/202206

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Mitoxantrone (NAP) - PSUSA/00002076/202206

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[19] Ophthalmic formulations only

6.3.19. Nitrous oxide (NAP); nitrous oxide, oxygen (NAP) - PSUSA/00010572/202206

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Pentamidine (NAP) - PSUSA/00002338/202206

Applicant(s): various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Phentermine, topiramate (NAP) - PSUSA/00010956/202207

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Ropinirole (NAP) - PSUSA/00002661/202207

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Sulfamethizole (NAP) - PSUSA/00010561/202206

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Theophylline (NAP) - PSUSA/00002921/202206

Applicant(s): various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Vespula SPP (802), wasp venom[20,21] (NAP) - PSUSA/00010721/202207

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/LEG 015.2

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 0015.1, Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) adopted in September 2021] as per the request for supplementary information (RSI) adopted in September 2022

Action: For adoption of advice to CHMP

6.4.2. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/LEG 010.2

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 010.1, Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) adopted in September 2021] as per as per the request for supplementary information (RSI) adopted in September 2022

Action: For adoption of advice to CHMP

6.4.3. Dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/LEG 005.2

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: David Olsen

Scope: MAH's response to LEG 005.1, Submission of all available data/results for study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of

[20] With or without adjuvant
[21] Allergen for diagnostic and/or therapy

people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) adopted in September 2021] as per the request for supplementary information (RSI) adopted in September 2022

Action: For adoption of advice to CHMP

6.4.4. Nirmatrelvir, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/REC 017.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: MAH's response to REC 017 [A safety review for myalgia covering safety data from ongoing early access worldwide and notably from US (Emergency Use Authorisation) and literature data with cut-off date 31st March should be provided by April 2022, awaiting for a global safety review planned to be submitted covering the 3 applicant's sponsored clinical studies (EPIC-HR, EPIC-SR and study in PEP) in June 2022 (requested by CHMP and assessed by PRAC)] as per the request for supplementary information (RSI) adopted in October[22] 2022

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0063, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Update of section 4.4 of the SmPC in order to update the warnings and precautions for myocardial infarction and ocular events following PSUR single assessment (PSUSA) procedure (PSUSA/00010498/202111) concluded in June 2022, based on the cumulative review of the relevant cases retrieved from the MAH's global safety database, clinical database, epidemiological evaluation and literature review. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

6.5.2. Laronidase - ALDURAZYME (CAP) - EMEA/H/C/000477/II/0085

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: To update section 4.2 of the SmPC in order to modify the administration instructions following the periodic safety update single assessment (PSUSA) procedure (PSUSA/00001830/202104) adopted in December[23] 2021 based on literature review. The package leaflet is updated accordingly. The RMP version 1.0 has also been submitted

Action: For adoption of PRAC Assessment Report

[22] Held 26-29 September 2022
[23] Held 29 November – 02 December 2021

6.6. Expedited summary safety reviews[24]

6.6.1. Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - EMEA/H/C/006019/MEA 009.5

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Sixth expedited summary safety report (SSR) for covid-19 vaccine (inactivated, adjuvanted) Valneva during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[25]

7.1.1. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/PSA/S/0092.1

Applicant: Blueprint Medicines

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to PSA/S/0092 [Substantial amendment to a protocol for BLU-285-1406: observational study evaluating safety and efficacy of avapritinib in the first line treatment of patients with Platelet derived Growth Factor Alpha D842V mutated gastrointestinal stromal tumour] as per the request for supplementary information (RSI) adopted in November[26] 2022

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

7.1.2. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/PSA/S/0102

Applicant: Kite Pharma EU B.V., ATMP[27]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Substantial amendment to a protocol for a long-term, non-interventional study of recipients of Yescarta for treatment of relapsed or refractory Diffuse Large B-cell Lymphoma and Primary Mediastinal B-cell Lymphoma

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

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

[25] In accordance with Article 107n of Directive 2001/83/EC

[26] Held on 24-27 October 2022

[27] Advanced therapy medicinal product

7.1.3. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/PSA/S/0086.1

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: MAH's response to PSA/S/0086 [Substantial amendment (version 8.0) to a protocol previously agreed in June 2022 (PSA/S/0082.1) for study TED-R13-002: a prospective, multicentre registry for patients with short bowel syndrome] as per the request for supplementary information (RSI) adopted in

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

7.1.4. Valproate[28] (NAP) - EMEA/H/N/PSA/J/0091.1

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

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to PSA/J/0091 [Substantial amendment to an agreed protocol for a non-interventional retrospective longitudinal study, conducted in the United Kingdom and France to evaluate and identify the best practices for switching of valproate and related substances in clinical practice [VALSE study (VALNAC09344)], as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate and related substances, completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in October[29] 2022

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[30]

7.2.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/MEA 002.6

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: MAH's response to MEA 002.4 [protocol amendment to include a cohort to Study D8220C00008: phase 3b, multicentre, open-label, single-arm in subjects with chronic lymphocytic leukaemia (ASSURE) to address missing information around moderate to severe cardiac impaired patients in subjects treated with Calquence(acalabrutinib)] as per the request for supplementary information (RSI) adopted in July 2022

Action: For adoption of advice to CHMP

7.2.2. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/MEA 035.5

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: MAH's response to MEA 35.4 [Amendment to a previously agreed protocol for study 20180204 (listed as category 3 study in the RMP): an observational registry study to evaluate the use and safety of

[28] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium
[29] Held 26-29 September 2022
[30] 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

cinacalcet among paediatric patients with secondary hyperparathyroidism] as per the request for supplementary information (RSI) adopted in October[31] 2022

Action: For adoption of advice to CHMP

7.2.3. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/MEA 002.4

Applicant: Merck Europe B.V.

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Amendment to a previously agreed protocol for study MS 700568-0002 (CLARION) (listed as category 3 study in the RMP): prospective, observational cohort study evaluating the safety profile, in terms of incidence of adverse events of special interest, in patients with highly active relapsing multiple sclerosis (RMS) newly started on oral cladribine

Action: For adoption of advice to CHMP

7.2.4. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/MEA 003.2

Applicant: Merck Europe B.V.

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Amendment to a previously agreed protocol for study MS700568-0004: Pregnancy outcomes in women exposed to oral cladribine: a multi-country cohort database study - CLEAR

Action: For adoption of advice to CHMP

7.2.5. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - EMEA/H/C/005737/MEA 010.3

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a revised protocol for VAC31518COV4001 (listed as category 3 study in the RMP): a post-authorisation, observational study to assess the safety of Ad26.COV2.S using health insurance claims and/or electronic health record (EHR) database(s) in the United States, including FDA feedback

Action: For adoption of advice to CHMP

7.2.6. Coronavirus (COVID-19) vaccine (B.1.351 variant, prefusion Spike delta TM protein, recombinant) - VIDPREVTYN BETA (CAP) - EMEA/H/C/005754/MEA 002

Applicant: Sanofi Pasteur

PRAC Rapporteur: Jana Lukacisinova

Scope: Submission of a protocol for study VAT 00007: Post-authorisation, observational study to assess the safety of VidPrevtyn Beta using routinely collected secondary data in Europe through VAC4EU. A non-interventional PASS to assess the occurrence of pre-specified AESIs and safety concerns following administration of VidPrevtyn Beta as a booster dose in a real-world setting

[31] Held 26-29 September 2022

Action: For adoption of advice to CHMP

7.2.7. Diroximel fumarate - VUMERITY (CAP) - EMEA/H/C/005437/MEA 002.2

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002.1 [protocol for 272MS403 (study number changed from Study SE-VUM-12146 to) (listed as category 3 study in the RMP): an observational study utilising data from 'big data' multiple sclerosis registries to evaluate the long-term safety of Vumerity (diroximel fumarate) and Tecfidera (dimethyl fumarate)] as per request for supplementary information (RSI) adopted in October 2022

Action: For adoption of advice to CHMP

7.2.8. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/MEA 002

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of a protocol for a PASS to characterise the risks and missing information outlined in the risk management plan including serious infections, use of live/attenuated vaccines, use with monoclonal antibodies, long-term safety and use in immunocompromised patients and evaluate whether there are specific and/or unexpected patterns of adverse events

Action: For adoption of advice to CHMP

7.2.9. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/MEA 004

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of a protocol for a PASS to characterise the missing information use in pregnant woman outlined in the risk management plan

Action: For adoption of advice to CHMP

7.2.10. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/MEA 005

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of a protocol for a PASS to characterise the missing information use in patients with moderate and severe renal impairment outlined in the risk management plan

Action: For adoption of advice to CHMP

7.2.11. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/MEA 006

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of a protocol for a PASS to characterise the missing information effect on vaccination efficacy outlined in the risk management plan

Action: For adoption of advice to CHMP

7.2.12. Fexinidazole - FEXINIDAZOLE WINTHROP (Art 58[32]) - EMEA/H/W/002320/MEA 002.2

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study FEXINC09395: a prospective observational study of the safety of fexinidazole for human African trypanosomiasis

Action: For adoption of advice to CHMP

7.2.13. Inclisiran - LEQVIO (CAP) - EMEA/H/C/005333/MEA 004.2

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

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

Action: For adoption of advice to CHMP

7.2.14. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/MEA 046.6

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 046.5 [Substantial amendment to a protocol previously endorsed in November 2017 for study CC-5013-MCL-005 to further investigate and characterise the association of lenalidomide and tumour flare reaction (TFR)/high tumour burden following the extension of indication for the treatment of adult patients with relapsed and/or refractory mantle cell lymphoma (RRMCL)] as per the request for supplementary information (RSI) adopted in September[33] 2022

Action: For adoption of advice to CHMP

7.2.15. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 067.2

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Amendment of protocol (v.9.0) for TOP study (Tysabri Observational Programme, Study Protocol

[32] 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)

[33] Held 29 august – 01 September 2022

IMA-06-02): a PASS, open-label, multinational, multicentre, prospective, observational study, to address the long-term safety profile and long-term impact on disease activity and progression of natalizumab with marketed use, and the impact of treatment on disability in particular by comparing the results with prospectively determined controls from established databases; the amendment aims to extend patient follow up from 10 to 15 years

Action: For adoption of advice to CHMP

7.2.16. Nirmatrelvir, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/MEA 008

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Initial protocol for study C4671037: use and safety of Paxlovid during pregnancy and among patients with moderate or severe hepatic or renal impairment

Action: For adoption of advice to CHMP

7.2.17. Nirmatrelvir, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/MEA 009.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Revised initial protocol for study C4671047: use and safety of Paxlovid among patients with moderate or severe hepatic or renal impairment

Action: For adoption of advice to CHMP

7.2.18. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 006.1

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: MAH's response to MEA 006 [Updated protocol for study 2019nCoV-404: US PASS to evaluate the pooled of risk of selected adverse events of special interest (AESI) within specified time periods after vaccination with Nuvaxovid using a claim and/or electronic healthcare record (her) database] as per the request for supplementary information (RSI) adopted in October[34] 2022

Action: For adoption of advice to CHMP

7.2.19. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/MEA 003.2

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of an updated study protocol (version 1.0) for study A4250-019 (listed as a category 3 study in the RMP): prospective registry-based study of the long-term safety of odevixibat in patients with progressive familial intrahepatic cholestasis (PFIC) to collect safety data on hepatotoxicity, diarrhoea, fat-

[34] Held 26-29 September 2022

soluble vitamins and fat-soluble nutrients in patients treated with odevixibat

Action: For adoption of advice to CHMP

7.2.20. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 004.1

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of updated protocol for study OMB157G2406: non-interventional study Kesimpta long-term retrospective safety study utilising real-world data from existing multiple sclerosis (MS) registries and databases from multiple countries, with primary objective is to estimate the event rates of malignancy and serious infections following ofatumumab treatment in patients with MS, and secondary objective to compare the incidence of each serious safety event between ofatumumab exposed patients with RMS and patients with RMS exposed to other approved disease modifying therapies (DMTs)

Action: For adoption of advice to CHMP

7.2.21. Pegcetacoplan - ASPAVELI (CAP) - EMEA/H/C/005553/MEA 002.1

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of revised protocol for study Sobi.PEGCET-301: non-imposed, non-interventional PASS using registry data for pegcetacoplan to evaluate the occurrence of serious infections in patients with paroxysmal nocturnal haemoglobinuria (PNH) treated with pegcetacoplan

Action: For adoption of advice to CHMP

7.2.22. Pegcetacoplan - ASPAVELI (CAP) - EMEA/H/C/005553/MEA 003.1

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: submission of revised protocol for study Sobi.PEGCET-302: non-imposed, non-interventional PASS for assessment of pregnancy outcomes in patients with paroxysmal nocturnal haemoglobinuria (PNH) exposed to pegcetacoplan during pregnancy

Action: For adoption of advice to CHMP

7.2.23. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 005.5

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of a revised protocol for study 165-504: a global, multicentre study to assess maternal, foetal and infant outcomes of exposure to Palynziq (pegvaliase) during pregnancy and breastfeeding

Action: For adoption of advice to CHMP

7.2.24. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 001.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 001 [Protocol for study BHV3000-402: a prospective, registry-based, observational study to assess maternal, fetal and infant outcomes following exposure to rimegepant together with a statistical analysis plan (SAP)] as per the request for supplementary information (RSI) adopted in September[35] 2022

Action: For adoption of advice to CHMP

7.2.25. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 002.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 002 [Protocol for study BHV3000-403: retrospective cohort study of pregnancy outcomes in women exposed to rimegepant during pregnancy together with a statistical analysis plan (SAP)] as per the request for supplementary information (RSI) adopted in September[36] 2022

Action: For adoption of advice to CHMP

7.2.26. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 003.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 003 [Submission of protocol for study BHV3000-408: a PASS of rimegepant in patients with migraine and a history of cardiovascular diseases together with a statistical analysis plan (SAP)] as per the request for supplementary information (RSI) adopted in October[37] 2022

Action: For adoption of advice to CHMP

7.2.27. Somatrogon - NGENLA (CAP) - EMEA/H/C/005633/MEA 001

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of a protocol for study C0311023: an active surveillance study to monitor the real-world long-term safety of somatrogon among paediatric patients in Europe

Action: For adoption of advice to CHMP

7.2.28. Valoctocogene roxaparvovec - ROCTAVIAN (CAP) - EMEA/H/C/005830/MEA 003

Applicant: BioMarin International Limited, ATMP[38]

[35] Held 29 August – 01 September 2022
[36] Held 29 August – 01 September 2022
[37] Held 26-29 September 2022
[38] Advanced Therapy Medicinal Product

PRAC Rapporteur: Menno van der Elst

Scope: To inform the impact of BMN 270 on fertility, general toxicity, teratology, and germline transmission in females of childbearing potential and establish an adequate waiting period after BMN 270 infusion following which female patients can become pregnant

Action: For adoption of advice to CAT and CHMP

7.2.29. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 015.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Submission of revised protocol for study P22-907 (listed as category 3 study in the RMP): a one-time, cross-sectional survey study evaluating the effectiveness of the DHPC and of the revised venetoclax SmPC among hematologists in select European countries

Action: For adoption of advice to CHMP

7.2.30. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 016.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope:Submission of a revised protocol for study P22-905 (listed as category 3 study in the RMP): a one-time, cross-sectional survey study to evaluate effectiveness of the patient card among adult patients recently treated with venetoclax for chronic lymphocytic leukemia (CLL)per usual care in select European countries

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[39]

7.3.1. Aprotinin (NAP) - EMEA/H/N/PSR/S/0030

Applicant: Nordic Group BV

PRAC Rapporteur: Jean-Michel Dogné

Scope: Nordic Aprotinin Patient Registry to record utilisation information on patients at cardiac surgery centers

Action: For adoption of recommendation to CMDh (or request for supplementary information (RSI)

7.3.2. Lumacaftor, ivacaftor – ORKAMBI (CAP) - EMEA/H/C/PSR/S/0039

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Final study report for an observational study to evaluate the utilisation patterns and long-term

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

effects of lumacaftor and ivacaftor combination therapy in patients with cystic fibrosis

Action: For adoption of recommendation to CHMP (or request for supplementary information (RSI)

7.4. Results of PASS non-imposed in the marketing authorisation(s)[40]

7.4.1. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/II/0077

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final report from the PASS study ALIROC08577: a non-interventional drug utilisation study of alirocumab in special populations using two U.S. healthcare databases

Action: For adoption of PRAC Assessment Report

7.4.2. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/WS2406/0049; empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/WS2406/0075; empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/WS2406/0068

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 4.4 of the SmPC in order to remove an existing warning on hepatic injury based on final results from the PASS 1245-96 listed as a category 3 study in the RMP for Jardiance and Synjardy; this is a PASS in patients with type 2 diabetes mellitus (T2DM) to assess the risk of acute liver injury, acute kidney injury and chronic kidney disease, severe complications of urinary tract infection, genital infections, and diabetic ketoacidosis among patients treated with empagliflozin compared to patients treated with DPP-4inhibitors. The RMP versions for Jardiance (RMP version 20.0), Synjardy (RMP version 13.0) and Glyxambi (RMP version 8.0) have also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet for Glyxambi (in fulfilment of MEA 003.9)

Action: For adoption of PRAC Assessment Report

7.4.3. Glycerol phenylbutyrate - RAVICTI (CAP) - EMEA/H/C/003822/II/0044, Orphan

Applicant: Immedica Pharma AB

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final report from study HZNP-RAV-401 (listed as category 3 study in the RMP): European Post-Authorisation Registry for Ravicti (glycerol phenylbutyrate) Oral Liquid in Partnership with the European Registry and Network for Intoxication Type Metabolic Diseases (E-IMD) The RMP version 7.4 has also been submitted

Action: For adoption of PRAC Assessment Report

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

7.4.4. Human papillomavirus 9-valent vaccine (recombinant, adsorbed) - GARDASIL 9 (CAP) - EMEA/H/C/003852/II/0063

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.6 of the SmPC in order to include additional information on exposure during pregnancy, based on the final report of the US Pregnancy Registry, listed as a category 3 study in the RMP; the package leaflet is updated accordingly. The RMP version 5.1 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.5. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/II/0056

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study GS-EU-313-4172 listed as a category 3 study in the RMP. This is a non-interventional study to assess the safety profile of idelalisib in patients with refractory follicular lymphoma (FL) with primary objective to assess the overall safety profile of idelalisib monotherapy in patients with refractory FL

Action: For adoption of PRAC Assessment Report

7.4.6. Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/II/0142

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study HUBIN-C-06380 listed as a category 3 study in the RMP. This is an observational prospective PASS designed to gain additional longitudinal and long-term safety data related to the use of Insuman Implantable 400 IU/mL via an IP implantable pump in a European observational cohort of patients with type 1 diabetes. The RMP version 5.0 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.7. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0054

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study NB-542 listed as a category 3 PASS in the RMP. This is a cross-sectional survey aimed to evaluate the effectiveness of the Mysimba Physician Prescribing Checklist (PPC) among physicians in the EU. The RMP version 12.6 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.8. Rituximab - RIXATHON (CAP) - EMEA/H/C/003903/WS2387/0063; RIXIMYO (CAP) - EMEA/H/C/004729/WS2387/0064

Applicant: Sandoz GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final report from study GP13-501 following procedure EMEA/H/C/PSUSA/00002652/201811. This is a prospective, open-label, single-arm, non-interventional, multicenter study describing the effectiveness and safety of biosimilar rituximab administered in combination with CHOP chemotherapy for the treatment of patients with previously untreated CD20-positive diffuse large B-cell lymphoma in current clinical practice

Action: For adoption of PRAC Assessment Report

7.4.9. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/II/0049

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final report for study 241501 listed as a category 2 study in the RMP in order to fulfil SOB/001.4. This is a prospective and retrospective, non-interventional PASS to evaluate the safety and effectiveness of Obizur in real-life practice. The RMP version 6.0 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.10. Vortioxetine - BRINTELLIX (CAP) - EMEA/H/C/002717/II/0037

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Jo Robays

Scope: Submission of the final report from study 16034N listed as a category 3 study in the RMP. This is a non-interventional PASS of vortioxetine in Europe: an analysis of European automated healthcare databases. The RMP version 4.0 has also been submitted

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. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/MEA 021

Applicant: Bayer AG

PRAC Rapporteur: Nathalie Gault

Scope: First annual safety report evaluating the intraocular pressure increase with the Eylea

Action: For adoption of advice to CHMP

7.5.2. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/ANX 010.7

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Interim report 2 for study DUT0008: non-interventional PASS to investigate drug utilisation and safety monitoring patterns for Lemtrada (alemtuzumab)

Action: For adoption of advice to CHMP

7.5.3. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/LEG 041.2

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: MAH's response to LEG 041.1 [Annual interim report year 11 for study 20090522: a PASS on denosumab global safety assessment among women with postmenopausal osteoporosis (PMO) and men with osteoporosis in multiple observational databases] as per the request for supplementary information (RSI) adopted in March

Action: For adoption of advice to CHMP

7.5.4. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 003.9

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Seventh interim report for study P903 (listed as a category 3 study in the RMP): a post authorisation safety study of Spikevax (elasomeran) in the US - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals

Action: For adoption of advice to CHMP

7.5.5. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 066.2

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: First interim report for study mRNA-1273-P911: long-term outcomes of myocarditis following administration of Spikevax (COVID-19 vaccine mRNA)

Action: For adoption of advice to CHMP

7.5.6. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 002.1

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002 [Progress report for study ZX008-1503: an open-label extension trial to assess the long-term safety of ZX008 (fenfluramine hydrochloride) oral solution as an adjunctive

therapy in children and young adults with Dravet syndrome] as per the request for supplementary information (RSI) adopted in October[41] 2022

Action: For adoption of advice to CHMP

7.5.7. Filgrastim - NIVESTIM (CAP) - EMEA/H/C/001142/MEA 015.7

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Sixth annual report for study ZOB-NIV-1513 (C1121008): a multinational, multicentre, prospective, non-interventional PASS in healthy donors (HDs) exposed to Nivestim (biosimilar filgrastim) for haematopoietic stem cell (HSC) mobilisation (NEST)

Action: For adoption of advice to CHMP

7.5.8. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 007.3

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Second interim report for study TEG4005: a pregnancy surveillance programme of infants and women exposed to Tegsedi (inotersen) during pregnancy

Action: For adoption of advice to CHMP

7.5.9. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/MEA 036.5

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 036.4 [Submission of the progress report for study CA184557: Long-term follow-up of ipilimumab treated paediatric patients enrolled in the Dutch melanoma treatment registry (DMTR)] as per the request for supplementary information (RSI) adopted in September[42] 2022

Action: For adoption of advice to CHMP

7.5.10. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/MEA 001.2

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Interim report for a PASS to characterise the safety of allogeneic haematopoietic stem cell transplantation (HSCT) in patients with cutaneous T-cell lymphoma (CTCL) treated with mogamulizumab

Action: For adoption of advice to CHMP

[41] Held 26-29 September 2022
[42] Held 29 August – 01 September 2022

7.5.11. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/MEA 004.2

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Interim report for study BA39730 (listed as a category 3 study in the RMP): a long term surveillance study to assess and characterize the long-term safety data from the use of ocrelizumab in treated patients with multiple sclerosis (MS)

Action: For adoption of advice to CHMP

7.5.12. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/ANX 001.5

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Fifth annual interim study report for study P15-11: a 5-year multicentre, observational PASS to document the utilisation of Wakix (pitolisant) in the treatment of narcolepsy with or without cataplexy and to collect information on its long-term safety when used in routine medical practice [final results expected in 2023]

Action: For adoption of advice to CHMP

7.5.13. Risdiplam - EVRYSDI (CAP) - EMEA/H/C/005145/MEA 007.3

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Interim results for study BN42833: a phase 4, non-interventional surveillance study for risdiplam [final study report expected in Q4/2031]

Action: For adoption of advice to CHMP

7.5.14. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005.6

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 005.5 [1) eighth annual progress report for pregnancy registry OBS13499 (US/CA): teriflunomide pregnancy outcome exposure registry: a 'teratology information specialists (OTIS)' autoimmune diseases in pregnancy project, 2) fifth annual progress report for OBS12751 (international): an international pregnancy exposure registry of women with multiple sclerosis (MS) exposed to Aubagio (teriflunomide)] as per request for supplementary information (RSI) adopted in October[43] 2022

Action: For adoption of advice to CHMP

7.5.15. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005.7

Applicant: Sanofi Winthrop Industrie

[43] Held 26-29 September 2022

PRAC Rapporteur: Martin Huber

Scope: 1) Ninth annual progress report for pregnancy registry OBS13499 (US/CA): teriflunomide pregnancy outcome exposure registry: a 'teratology information specialists (OTIS)' autoimmune diseases in pregnancy project, 2) Sixth annual progress report for OBS12751 (international): an international pregnancy exposure registry of women with multiple sclerosis (MS) exposed to Aubagio (teriflunomide)

Action: For adoption of advice to CHMP

7.5.16. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/ANX 002.3

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to ANX 002.2 [interim report for study 156-12-299: a non-interventional PASS to investigate the risks of hepatotoxicity, basal cell carcinoma and glaucoma associated with the use of Jinarc (tolvaptan). In addition, the study investigates pregnancy outcomes in patients treated with Jinarc (tolvaptan), patterns of medicinal product utilisation especially with regards to off-label use and use in patients over 50 years old as well as adverse drug reactions (ADRs) associated with long term use of Jinarc (tolvaptan) [final clinical study report (CSR) expected by: Q1/2026]] as per the request for supplementary information (RSI) adopted in September[44] 2020

Action: For adoption of advice to CHMP

7.5.17. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 037.3

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Monitoring report for study C4591009: a non-interventional PASS in US to assess the occurrence of safety events of interest, including myocarditis and pericarditis, among individuals in the general US population and in subcohorts of interest within selected data sources participating in the US Sentinel System

Action: For adoption of advice to CHMP

7.5.18. Turoctocog alfa pegol - ESPEROCT (CAP) - EMEA/H/C/004883/ANX 001.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Second study progress report for study NN7088-4029: A multinational, prospective, open labelled, non-controlled, non-interventional post-authorisation study of turoctocog alfa pegol (N8-GP) during long-term routine prophylaxis and treatment of bleeding episodes in patients with haemophilia A

Action: For adoption of advice to CHMP

[44] Held 31 August – 03 September 2022

7.6. Others

7.6.1. Radium (Ra^{223}) - XOFIGO (CAP) - EMEA/H/C/002653/ANX 013.3

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: MAH's response to ANX 013.2 [Request for deletion of ANX 013.1 post-approval commitment (study 20511): an open-label, multicentre, non-randomised Phase 1 study that has been requested by the European Commission as a result of the referral procedure (EMEA/H/A-20/1459/C/002653/0028) to further characterize the correlation between the extent of the disease, the dose and the distribution of radium-223 in bone metastases versus sites of impaired bone health versus normal bone structure] as per the request for supplementary information adopted in October[45] 2022

Action: For adoption of advice to CHMP

7.6.2. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 037.4

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Administrative letter update for clinical study to capture safety events (based on AESI) including myocarditis and pericarditis, in individuals of any age who received tozinameran since its availability under an EUA using electronic health records and claims data from data partners participating in the Sentinel System (study C4591009)

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

7.8. Ongoing Scientific Advice

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

[45] Held 26-29 September 2022

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Cerliponase alfa - BRINEURA (CAP) - EMEA/H/C/004065/S/0038 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Mari Thorn

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Cholic acid - ORPHACOL (CAP) - EMEA/H/C/001250/S/0048 (without RMP)

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0032 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Obiltoxaximab - NYXTHRACIS (CAP) - EMEA/H/C/005169/S/0008 (without RMP)

Applicant: SFL Pharmaceuticals Deutschland GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.5. Tocofersolan - VEDROP (CAP) - EMEA/H/C/000920/S/0044 (without RMP)

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

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. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/R/0034 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Mosunetuzumab - LUNSUMIO (CAP) - EMEA/H/C/005680/R/0001 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Selumetinib - KOSELUGO (CAP) - EMEA/H/C/005244/R/0010 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/R/0056 (with RMP)

Applicant: Kite Pharma EU B.V., ATMP[46]

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.3.2. Binimetinib - MEKTOVI (CAP) - EMEA/H/C/004579/R/0024 (without RMP)

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

[46] Advanced Therapy Medicinal Product

8.3.3. Caplacizumab - CABLIVI (CAP) - EMEA/H/C/004426/R/0042 (without RMP)

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - EMEA/H/C/004282/R/0037 (without RMP)

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Deferiprone - DEFERIPRONE LIPOMED (CAP) - EMEA/H/C/004710/R/0011 (with RMP)

Applicant: Lipomed GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/R/0055 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Encorafenib - BRAFTOVI (CAP) - EMEA/H/C/004580/R/0029 (without RMP)

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Eravacycline - XERAVA (CAP) - EMEA/H/C/004237/R/0023 (with RMP)

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Lipegfilgrastim - LONQUEX (CAP) - EMEA/H/C/002556/R/0077 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Nitisinone - NITYR (CAP) - EMEA/H/C/004582/R/0015 (with RMP)

Applicant: Cycle Pharmaceuticals (Europe) Limited

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/R/0031 (without RMP)

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Pomalidomide - IMNOVID (CAP) - EMEA/H/C/002682/R/0049 (without RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Monica Martinez Redondo

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/R/0068 (without RMP)

Applicant: Novartis Europharm Limited, ATMP[47]

PRAC Rapporteur: Gabriele Maurer

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

[47] Advanced therapy medicinal product

8.3.14. Vonicog alfa - VEYVONDI (CAP) - EMEA/H/C/004454/R/0027 (with RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Hydroxychloroquine (NAP) - DK/H/PSUFU/00001693/202104 PSUFU

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen Scope: PRAC consultation on the need for further evaluation of the risk of hepatotoxicity and teratogenicity, and/or any labelling updates for hydroxychloroquine, as per the conclusions of the PSUSA procedure follow-up measure (PSUFU) (EMA/PRAC/693177/2021) (DK/H/PSUFU/00001693/202104 PSUFU) concluded in February 2022, on request of Denmark

Action: For adoption of advice to Member States

11.1.2. Lisdexamfetamine (NAP) - SE/H/1839/01-06/II/40; SE/H/1825/0103/II/29

Applicant(s): Shire Pharmaceuticals Ireland Limited

PRAC Lead: Ulla Wandel Liminga

Scope: PRAC consultation on type II variations evaluating the risk of intestinal ischaemia, increased bleeding tendency and vasoconstriction/vasospasm as per conclusions of the PSUSA procedure (PSUSA/00010289/202202) concluded in October 2022, on request of Sweden

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q4 2022

Action: For information

12.1.3. Vote by proxy

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Oncology European Specialised Expert Community (ESEC) - update and request for nominations

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. PRAC workload statistics – Q4 2022

Action: For discussion

12.8.2. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q4 2022 and predictions

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla**Action:** For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. EudraVigilance Expert Working Group (EV-EWG) - work programme 2023-2024

Action: For adoption

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. 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. Impact of pharmacovigilance activities

12.20.1. Study report on the impact of EU label changes for fluoroquinolone-containing medicinal products for systemic and inhalation use: post-referral prescribing trends – follow up

PRAC lead: Martin Huber, Eva Jirsová

Action: For adoption

12.20.2. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact – revision of the process for prioritisation and follow-up of impact research – follow up

Action: For adoption

12.21. Others

12.21.1. Data analysis and real world interrogation network (DARWIN EU) – update

Action: For discussion

12.21.2. DARWIN EU – Drug utilisation study of antibiotics in the 'Watch' category of the WHO AwaRe classification of antibiotics for evaluation and monitoring of use

Action: For discussion

12.21.3. DARWIN EU - Study on drug utilisation of valproate-containing medicinal products in women of childbearing potential (EUPAS50789)

Action: For discussion

12.21.4. EMA-funded study on spinal muscular atrophy disease (SMA)

Action: For information

13. Any other business

Next meeting on: 13-16 March 2023

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/