14 April 2023
EMA/CHMP/58860/2023
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 23-26 January 2023

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

Health and safety information

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

Disclaimers

Some of the information contained in this set of minutes 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 vary during the course of the review. Additional details on some of these procedures will be published in the CHMP meeting highlights once the procedures are finalised and start of referrals will also be available.

Of note, these minutes a working document primarily designed for CHMP members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes 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).

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1. Introduction

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

The Chairperson opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) pandemic, and the associated EMA Business Continuity Plan (BCP), the meeting was held in-person with some members connected remotely (hybrid setting).

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics.

Participants were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared. Restrictions applicable to this meeting are captured in the list of participants included in the minutes.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The Chair announced the start of the Swedish presidency of the Council of the European Union (EU).

The CHMP was reminded that the majority is reduced to 16, as long as the 5th co-opted member position is vacant (see 14.1.2).

1.2. Adoption of agenda

CHMP agenda for 23-26 January 2023.

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 12-15 December 2022.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 16 January 2023.

The CHMP adopted the CHMP minutes for 12-15 December 2022.

The CHMP adopted the minutes from the PROM meeting held on 16 January 2023.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. pegunigalsidase alfa - Orphan - EMEA/H/C/005618

Chiesi Farmaceutici S.p.A.; treatment of Fabry disease

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday 24 January 2023 at 09:00

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

The CHMP agreed that an oral explanation was not needed at this time.

See 3.2

2.1.2. vadadustat - EMEA/H/C/005131

treatment of anaemia

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday 24 January 2023 at 16:00

List of Outstanding Issues adopted on 15.12.2022, 15.09.2022. List of Questions adopted on 24.03.2022.

An oral explanation was held on 24 January 2023. The presentation by the applicant focused on the clinical data in support of the application.

See 3.2

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Dapagliflozin Viatris - dapagliflozin - EMEA/H/C/006006

Viatris Limited; treatment of type 2 diabetes mellitus, heart failure and chronic kidney disease

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Forxiga

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.2. Sitagliptin/Metformin hydrochloride SUN - sitagliptin / metformin hydrochloride - EMEA/H/C/005778

Sun Pharmaceutical Industries Europe B.V.; treatment of type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Janumet

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The legal status was agreed as medicinal product subject to medical prescription.

The CHMP noted the letter of recommendation dated 25 January 2023.

The summary of opinion was circulated for information.

3.1.3. Sohonos - palovarotene - Orphan - EMEA/H/C/004867

Ipsen Pharma; treatment of fibrodysplasia ossificans progressiva

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 15.09.2022. List of Questions adopted on 16.09.2021.

The Committee adopted a negative opinion by consensus recommending the refusal of the granting of the marketing authorisation. The CHMP assessment report was adopted.

The question-and-answer document was circulated for information.

3.1.4. Sotyktu - deucravacitinib - EMEA/H/C/005755

Bristol-Myers Squibb Pharma EEIG; treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 15.12.2022, 21.07.2022. List of Questions adopted on 24.02.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that deucravacitinib is a new active substance, as claimed by the applicant.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.5. Tolvaptan Accord - tolvaptan - EMEA/H/C/005961

Accord Healthcare S.L.U.; treatment of hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Samsca

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 22.04.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.2. Initial applications; List of outstanding issues (Day 180; Day 120 for procedures with accelerated assessment timetable)

3.2.1. aripiprazole - EMEA/H/C/005929

Maintenance treatment of schizophrenia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 13.10.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.2. ublituximab - EMEA/H/C/005914

treatment of relapsing forms of multiple sclerosis (RMS)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.04.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.3. dabigatran etexilate - EMEA/H/C/005639

prevention of venous thromboembolic events

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 15.09.2022, 23.06.2022, 24.02.2022. List of Questions adopted on 12.11.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 4th list of outstanding issues.

The CHMP did not agree to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues.

3.2.4. pegunigalsidase alfa - Orphan - EMEA/H/C/005618

Chiesi Farmaceutici S.p.A.; treatment of Fabry disease

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

See 2.1

The Committee was reminded of the status of this application and its remaining outstanding issues.

The CHMP agreed that an oral explanation was not needed at this time.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

3.2.5. mirikizumab - EMEA/H/C/005122

treatment of moderately to severely active ulcerative colitis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.09.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.6. vadadustat - EMEA/H/C/005131

treatment of anaemia

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 15.12.2022, 15.09.2022. List of Questions adopted on 24.03.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

See 2.1

An oral explanation was held on 24 January 2023. The presentation by the applicant focused on the clinical data in support of the application.

The Committee adopted a 3rd list of outstanding issues with a specific timetable.

3.2.7. ganaxolone - Orphan - EMEA/H/C/005825

Marinus Pharmaceuticals Emerald Limited; treatment of epileptic seizures associated with cyclindependent kinase-like 5 deficiency disorder (CDD)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.01.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.3. Initial applications; List of questions (Day 120; Day 90 for procedures with accelerated assessment timetable)

3.3.1. recombinant respiratory syncytial virus pre-fusion F protein, adjuvanted with AS01E - EMEA/H/C/006054

Accelerated assessment

indicated for active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by RSV

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.2. latanoprost - EMEA/H/C/005933

Reduction of elevated intraocular pressure (IOP)

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.3. dabrafenib - Orphan - EMEA/H/C/005885

Novartis Europharm Limited; Treatment of glioma

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.4. leniolisib - Orphan - EMEA/H/C/005927

Pharming Technologies B.V.; Treatment of activated phosphoinositide 3-kinase delta syndrome (APDS)

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.5. trametinib - Orphan - EMEA/H/C/005886

Novartis Europharm Limited; Treatment of paediatric patients aged 1 year and older with glioma

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.6. tocilizumab - EMEA/H/C/005984

treatment of rheumatoid arthritis, active systemic juvenile idiopathic arthritis (sJIA), juvenile idiopathic polyarthritis (pJIA), chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS) and COVID-19

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.7. fezolinetant - EMEA/H/C/005851

treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with

the list of questions.

3.3.8. zilucoplan - Orphan - EMEA/H/C/005450

UCB Pharma S.A.; treatment of generalised myasthenia gravis in adults

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.4. Update on on-going initial applications for Centralised procedure

3.4.1. crisantaspase - EMEA/H/C/005917

Indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukaemia (ALL) and lymphoblastic lymphoma (LBL).

Scope: Letter by the applicant dated 10.01.2023 requesting an extension to the clock stop to respond to the list of questions adopted in October 2022.

Action: For adoption

List of Question adopted on 13.10.2022

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in October 2022.

3.4.2. bevacizumab - EMEA/H/C/005574

treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer; first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer; first-line treatment of patients with advanced and/or metastatic renal cell cancer.

Scope: Letter by the applicant dated 21.12.2022 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in February 2022.

Action: For adoption

List of Outstanding Issues adopted on 24.02.2022. List of Questions adopted on 22.04.2021.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in February 2022.

3.4.3. daprodustat - EMEA/H/C/005746

treatment of anaemia associated with chronic kidney disease (CKD) in adults

Scope: Letter by the applicant dated 04.01.2023 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2022.

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in November 2022.

3.4.4. dantrolene sodium, hemiheptahydrate - Orphan - EMEA/H/C/006009

Norgine B.V.; treatment of malignant hyperthermia (including suspected cases)

Scope: Letter by the applicant dated 18.01.2023 requesting an extension to the clock stop to respond to the list of questions adopted in November 2022.

Action: For adoption

List of Questions adopted on 10.11.2022.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in November 2022.

3.5. Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

4.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion

4.1.1. Byfavo - remimazolam - EMEA/H/C/005246/X/0002

Paion Deutschland GmbH

Rapporteur: Bruno Sepodes, Co-Rapporteur: Selma Arapovic Dzakula, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension application to introduce a new pharmaceutical form associated with a new strength (50 mg powder for concentrate for solution for injection/infusion). The new presentation is indicated to include the intravenous induction and maintenance of general anaesthesia (GA) in adults for Byfavo 50 mg, based on final results from two pivotal trials: Study ONO-2745-05, a phase IIb/III, single-blind, randomised, parallel-group study assessing safety and efficacy in induction and maintenance of anaesthesia in ASA I/II patients (general surgery), and study CNS-7056-022, a phase III, randomized, propofol controlled, parallel group, confirmatory single-blind efficacy and safety trial during induction and maintenance of anaesthesia in ASA III/IV patients.
A new combined version of the SmPC, labelling and Package Leaflet solely for the 50 mg strength and the GA indication is provided accordingly.
Version 1.3 of the RMP has also been approved within this procedure."

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 19.05.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

4.1.2. Hefiya - adalimumab - EMEA/H/C/004865/X/0036/G

Sandoz GmbH

Rapporteur: Christian Gartner, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength (80 mg/0.8 mL) of the solution for injection grouped with quality variations. The Package Leaflet and Labelling are updated in accordance.
The RMP (version 9.0) has also been submitted.
Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in the List of All Authorised Presentations (Annex A) to differentiate packs of pre-filled syringes with or without needle safety device."

Action: For adoption

List of Questions adopted on 13.10.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

4.1.3. Hyrimoz - adalimumab - EMEA/H/C/004320/X/0036/G

Sandoz GmbH

Rapporteur: Christian Gartner, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength (80 mg/0.8 mL) of the solution for injection grouped with quality variations. The Package Leaflet and Labelling are updated in accordance.
The RMP (version 9.0) has also been submitted.
Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in the List of All Authorised Presentations (Annex A) to differentiate packs of pre-filled syringes with or without needle safety device."

Action: For adoption

List of Questions adopted on 13.10.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

4.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 list of outstanding issues

4.2.1. Ultomiris - ravulizumab - EMEA/H/C/004954/X/0027/G

Alexion Europe SAS

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection) associated with new strength (245 mg) and route of administration (subcutaneous use), grouped with a type II variation (C.I.4) to align the summary of product characteristics and labelling of Ultomiris intravenous formulation (IV) with the proposed Ultomiris subcutaneous formulation (SC). The RMP (version 5.0) is updated in accordance."

Action: For adoption

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 21.07.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues, relating to clinical aspects.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

4.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of question

4.3.1. Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/X/0016

Novo Nordisk A/S

Rapporteur: Daniela Philadelphy

Scope: "Extension application to add two new strengths of 4000 IU and 5000 IU powder and solvent for solution for injection."

Action: For adoption

The Committee discussed the issues identified in this application, relating to quality, non-clinical and clinical aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.3.2. Ofev - nintedanib - EMEA/H/C/003821/X/0052/G

Boehringer Ingelheim International GmbH

Rapporteur: Finbarr Leacy, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension application to add a new strength of 25 mg soft capsule grouped with a type II variation C.I.6.a to add a new indication of treatment of fibrosing Interstitial Lung Diseases (ILDs) in children and adolescents from 6 to 17 years of age, based on results from study 1199 0337 (InPedILD); a randomised, placebo-controlled, double-blind, multicentre, multinational, phase III clinical trial undertaken to evaluate dose-exposure and safety of nintedanib on top of standard of care in children and adolescents (6 to 17 years old) with clinically significant fibrosing ILD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes to the list of local representatives in the Package Leaflet. The updated RMP version 12.0 is also submitted."

Action: For adoption

The Committee discussed the issues identified in this application, relating to quality and clinical aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.3.3. Olumiant - baricitinib - EMEA/H/C/004085/X/0035/G

Eli Lilly Nederland B.V.

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension application to introduce a new strength (1 mg film-coated tablet),

grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment, as monotherapy or in combination with conventional synthetic disease modifying antirheumatic drugs (DMARDs), of active juvenile idiopathic arthritis (JIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more prior conventional synthetic or biologic DMARDs, based on final results from the pivotal study JAHV (I4V-MC-JAHV); this is a multicentre, double-blind, randomised, placebo-controlled, medication-withdrawal Phase 3 study in children from 2 years to less than 18 years of age with JIA who have had an inadequate response or intolerance to treatment with at least 1 cDMARD or bDMARD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 15.1 of the RMP has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, relating to quality and clinical aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.3.4. Viagra - sildenafil - EMEA/H/C/000202/X/0115

Upjohn EESV

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro

Scope: "Extension application to introduce a new pharmaceutical form (orodispersible film)."

Action: For adoption

The Committee discussed the issues identified in this application, relating to quality and clinical aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008

No items

4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

No items

5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008

5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information

5.1.1. Dupixent - dupilumab - EMEA/H/C/004390/II/0060

Sanofi Winthrop Industrie

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to include treatment of atopic dermatitis in paediatric patients from 6 months to <6 years of age based on final results from study R668-AD-1539; this is a phase 2/3 study investigating the pharmacokinetics, safety and efficacy of dupilumab in patients aged ≥6 months to <6 years with moderate-to-severe atopic dermatitis.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 13.10.2022, 23.06.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

5.1.2. Nubeqa - darolutamide - EMEA/H/C/004790/II/0009

Bayer AG

Rapporteur: Alexandre Moreau, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension of indication to include treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel, based on final results from study 17777 (ARASENS); this is a randomized, double-blind, placebo-controlled Phase 3 study designed to demonstrate the superiority of darolutamide in combination with docetaxel over placebo in combination with docetaxel in OS in patients with mHSPC. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. As part of the application, the MAH is also requesting one additional year of market protection.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 15.12.2022, 15.09.2022, 23.06.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

5.1.3. Reblozyl - luspatercept - Orphan - EMEA/H/C/004444/II/0009

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Daniela Philadelphy, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Jo Robays

Scope: "C.I.6 (Extension of indication)
Extension of indication in β-thalassaemia to include adult patients with non-transfusion dependent β-thalassaemia (NTDT) for Reblozyl; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 15.12.2022, 10.11.2022, 23.06.2022, 27.01.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

5.1.4. Rinvoq - upadacitinib - EMEA/H/C/004760/II/0027

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include treatment of moderately to severely active Crohn's disease in adult patients for Rinvoq, based on final results from three Phase III studies, two confirmatory placebo-controlled induction studies (study M14 431/U-EXCEED/CD-1 and study M14 433/U-EXCEL/CD-2) and a placebo-controlled maintenance/long-term extension study (study M14-430/U-ENDURE/CD-3).
M14-431 study is a Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Induction Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Moderately to Severely Active Crohn's Disease Who Have Inadequately Responded to or are Intolerant to Biologic Therapy.

M14-433 study is a Phase III, Multicenter, Randomized, Double-Blind, Placebo Controlled Induction Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Moderately to Severely Active Crohn's Disease Who Have Inadequately Responded to or are Intolerant to Conventional and/or Biologic Therapies.
M14-430 study is an ongoing Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Maintenance and Long-Term Extension Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Crohn's Disease Who Completed the Studies M14-431 or M14-433.
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 11 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 10.11.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.5. TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0117

Corza Medical GmbH

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of children aged 1 month to 18 years, based on available bibliographical data, results from study TC-2402-040-SP which compared TachoSil with Surgicel Original as adjunct to primary surgical treatment in both adult and paediatric subjects, and results from study TC-019-IN; a prospective, uncontrolled study in paediatric subjects. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in the product information. Version 0.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.6. Trecondi - treosulfan - Orphan - EMEA/H/C/004751/II/0014

medac Gesellschaft fur klinische Spezialpraparate mbH

Rapporteur: Fátima Ventura, PRAC Rapporteur: Julia Pallos

Scope: "Extension of indication to include additional non-malignant transplant indications (non-malignant diseases in the paediatric population) for Trecondi 1 g/5 g powder for solution for infusion based on final 12-months follow-up results of study MC-FludT.16/NM; a

randomised phase II interventional study aimed to compare treosulfan-based conditioning therapy with Busulfan-based conditioning prior to allogeneic haematopoietic stem cell transplantation in paediatric patients with non-malignant diseases.
Further, the MAH proposes to amend an existing warning on skin toxicity based on new literature data. Moreover, the MAH proposes to introduce a slightly modified dosing regimen according to the patient's body surface based on long-term follow-up data of paediatric study MC-FludT.17/M, a Phase II trial to describe the safety and efficacy of treosulfan based conditioning therapy prior to allogeneic haematopoietic stem cell transplantation in paediatric patients with haematological malignancies, as well as a final analysis of the population pharmacokinetics of treosulfan in paediatric patients. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 10.11.2022, 21.07.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

5.1.7. Trulicity - dulaglutide - EMEA/H/C/002825/II/0065

Eli Lilly Nederland B.V.

Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include treatment of type 2 diabetes mellitus (T2DM) in children and adolescents aged 10 to less than 18 years based on final results from study H9X-MC-GBGC; this is a phase 3, double-blind, randomised, multi-centre, placebo-controlled superiority trial to evaluate PK, PD, safety and efficacy of dulaglutide in children from 10 to less than 18 years of age, with an open label extension to evaluate safety. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 13.10.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

5.1.8. Valdoxan - agomelatine - EMEA/H/C/000915/II/0051

Les Laboratoires Servier

Rapporteur: Eva Skovlund, PRAC Rapporteur: Pernille Harg

Scope: "Extension of indication to include a new therapeutic indication in adolescents aged 12 to 17 years for the treatment of moderate to severe major depressive episodes, if depression is unresponsive to psychological therapy alone, for Valdoxan, further to the results of the phase 2 (CL2-20098-075) and phase 3 (CL3-20098-076) paediatric clinical studies included in the Paediatric Investigation Plan number EMEA-001181-PIP-11; As a consequence, the sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated.
The Package Leaflet is updated accordingly. The updated RMP version 25.1 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.9. Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0040

Gilead Sciences Ireland UC

Rapporteur: Janet Koenig, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Valentina Di Giovanni

Scope: "Extension of indication to include treatment of chronic hepatitis B-infected children from 6 years and older and weighing at least 25 kilograms for Vemlidy, based on the interim results from Week 24 clinical study report (CSR) for Cohort 1 and Cohort 2 Group 1 and supporting modular summaries for the category 3 study GS-US-320-1092, 'A Randomized, Double-Blind Evaluation of the Pharmacokinetics, Safety and Antiviral Efficacy of Tenofovir Alafenamide (TAF) in Children and Adolescent Subjects with Chronic Hepatitis B Virus Infection'. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the MAH took the opportunity to update the wording in section 4.6 of the SmPC related to breastfeeding and pregnancies exposed to TAF, and to update the contact details of the local representative in Romania in the Package Leaflet. An updated RMP version 8.2 has been provided."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.10. Wakix - pitolisant - Orphan - EMEA/H/C/002616/II/0030

Bioprojet Pharma

Rapporteur: Jean-Michel Race, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension of indication to include treatment of narcolepsy with or without cataplexy in adolescents and children from the age of 6 years, based on results from study P11-06;

an ongoing phase III, double-blind, multicentre, randomized, placebo-controlled trial undertaken to evaluate safety and efficacy of pitolisant in children from 6 to less than 18 years with narcolepsy with/without cataplexy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

No items

5.3. Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

No items

6. Medical devices

6.1. Ancillary medicinal substances - initial consultation

No items

6.2. Ancillary medicinal substances – post-consultation update

No items

6.3. Companion diagnostics - initial consultation

6.3.1. in vitro diagnostic medical device - EMEA/H/D/006201

to detect internal tandem duplication (ITD) and tyrosine kinase domain (TKD) mutations D835 and I836

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

6.4. Companion diagnostics – follow-up consultation

No items

7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. danicopan - H0005517

Paroxysmal nocturnal hemoglobinuria (PNH)

Scope: Briefing note and the Rapporteurs' recommendation on the request for accelerated assessment.

Action: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.2. respiratory syncytial virus vaccine - EMEA/H/C/006027

prevention of respiratory tract disease

Scope: Briefing note and the Rapporteurs' recommendation on the request for accelerated assessment.

Action: For adoption

The CHMP agreed to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.2. Priority Medicines (PRIME)

Information related to priority medicines cannot be released at present time as these

contain commercially confidential information.

8.2.1. List of applications received

Action: For information

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 6 recommendations for eligibility to PRIME: 2 were accepted and 4 were denied.

The individual outcomes are listed in the PRIME Monthly Report on the EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Lynparza - olaparib - EMEA/H/C/003726/II/0058

AstraZeneca AB

Rapporteur: Alexandre Moreau

Scope: "Update of section 5.1 of the SmPC in order to provide the Final Overall Survival (OS) Analysis from study D0816C00020 (OPINION). This is a Phase IIIb single-arm, open-label, multicentre study of maintenance therapy in PSR non-germline BRCA mutated ovarian cancer patients who are in complete or partial response following platinum-based chemotherapy."

Action: For adoption

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

9.1.2. Kogenate Bayer – octocog alfa – EMEA/H/C/000275

Bayer AG

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Filip Josephson

Scope: Expiry of marketing authorisation due to Sunset Clause

Action: For information

The CHMP noted the expiry of marketing authorisation.

9.1.3. Pazenir – paclitaxel – EMEA/H/C/004441

Ratiopharm GmbH

Rapporteur: Daniela Philadelphy

Scope: DHPC and communication plan

The DHPC and communication plan have been adopted via written procedure on 12 January 2023.

Action: For information

The CHMP noted the DHPC and communication plan which had been adopted via written procedure on 12 January 2023.

9.1.4. Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0056

Orexigen Therapeutics Ireland Limited

Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber

Scope: "Submission of updated study design and protocol synopsis for the CVOT-2 study, a category 1 study listed in Annex II.D (ANX/001.7) undertaken to assess the effect of naltrexone extended release (ER) / bupropion ER on the occurrence of major adverse cardiovascular events (MACE), as requested in the CHMP AR for ANX/001.6. The Annex II and the RMP version 13 are updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022, 24.03.2022.

The Committee discussed the issues identified in this application, relating to clinical aspects.

The Committee adopted a 3rd request for supplementary information with a specific timetable.

9.1.5. Translarna - ataluren - EMEA/H/C/002720/II/0069, Orphan

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information following results from study PTC124-GD-041-DMD, listed as a specific obligation in the Annex II; This is a Phase 3 multicentre, randomised, double-blind, 18-month, placebo-controlled study, followed by a 18-month open label extension to confirm the efficacy and safety of ataluren in the treatment of ambulant patients with mnDMD aged 5 years or older.
Annex II and Annex IIB are updated to delete the SOB and to reflect the switch from conditional to full marketing authorisation. The Package Leaflet is updated accordingly.
The RMP version 11.0 has also been submitted. Minor corrections were done to align the PI with the latest QRD templates."

Request to switch to standard MA.

Action: For adoption

The Committee discussed the issues identified in this application, relating to clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

9.1.6. Adakveo - crizanlizumab - Orphan - EMEA/H/C/004874

Novartis Europharm Limited; treatment of sickle cell disease.

Rapporteur: Daniela Philadelphy, Co-Rapporteur: Johanna Lähteenvuo, PRAC Rapporteur: Laurence de Fays

Scope: Update on the product

Action: For discussion

The CHMP was informed that first interpretable results of the study A2301 did not show evidence of superiority of either dose of crizanlizumab (5.0 mg/kg or 7.5mg/kg) over the placebo on the primary and key secondary endpoints.

See 10.1

9.1.7. Rubraca - rucaparib - EMEA/H/C/004272/II/0037

Clovis Oncology Ireland Limited

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information and the list of adverse drug reactions (ADRs) based on the final results from study CO-338-014 (ARIEL 3) listed as a category 1 PAES in the Annex II; this is a phase 3, multicenter, randomized, double-blind, placebo-controlled study of rucaparib as switch maintenance following platinum-based chemotherapy in patients with platinum-sensitive, high grade serous or endometrioid epithelial ovarian, primary peritoneal or fallopian tube cancer. The Package Leaflet is updated accordingly. The RMP version 6.4 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Update on procedure.

Action: For information

CHMP noted the updated on the status of this application.

9.1.8. Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0019/G

Pfizer Europe MA EEIG

Rapporteur: Jean-Michel Race

Scope: quality variation

Action: For adoption

Request for Supplementary Information adopted on 13.10.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

9.1.9. Sirturo - bedaquiline - EMEA/H/C/002614/II/0051, Orphan

Janssen-Cilag International N.V.

Rapporteur: Filip Josephson

Scope: "Update of section 4.6 of the SmPC in order to update information on breast-feeding based on new literature."

Action: For adoption

Request for Supplementary Information adopted on 15.12.2022.

The Committee discussed the issues identified in this application, relating to clinical aspects.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

9.1.10. Vaxneuvance - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477/II/0011

Merck Sharp & Dohme B.V.

Rapporteur: Johann Lodewijk Hillege

Scope: "To update sections 4.2 and 5.1 of the SmPC in order to update the information for immune response after subcutaneous administration based on final results from study V114-P033 (EudraCT: 2019-003644-68), in accordance with Article 46 of the paediatric regulation. V114-P033 is a phase 3 Active-Comparator controlled study to evaluate the Safety, Tolerability and Immunogenicity of V114 in Healthy Japanese Infants.
The Package Leaflet is updated accordingly."

Action: For adoption

The Committee discussed the issues identified in this application, relating to clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

9.1.11. WS2307/ Rixathon-EMEA/H/C/003903/WS2307/0062 Riximyo-EMEA/H/C/004729/WS2307/0063

Sandoz GmbH

Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Anette Kirstine Stark

Scope: "Update of section 4.1 of the SmPC in order to include the rapid infusion regimen (90 minutes) for second and subsequent infusions in the label for patients with non-Hodgkin's lymphoma (NHL) or chronic lymphocytic leukaemia (CLL) based on non-interventional PASS CGP2013ES01R and scientific literature. The RMP version 7.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

9.1.12. Fasturtec – rasburicase – EMEA/H/C/000331

Sanofi Winthrop Industrie

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alexandre Moreau

Scope: DHPC and communication plan

Action: For adoption

The CHMP adopted the DHPC and communication plan.

9.1.13. Livogiva – teriparatide - EMEA/H/C/005087/II/0010

Theramex Ireland Limited

Rapporteur: Daniela Philadelphy

Scope: quality variation

Request by the MAH dated 23 January 2023, requesting an extension to the clock stop to respond to the RSI adopted in September 2022.

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022, 23.06.2022.

The CHMP did not agree to the request by the MAH for an extension to the clock stop to respond to the RSI adopted in September 2022.

10. Referral procedures

10.1. Procedure for Centrally Authorised products under Article 20 of Regulation (EC) No 726/2004

10.1.1. Janus kinase (JAK) inhibitors[1]: abrocitinib - CIBINQO (CAP); baricitinib - OLUMIANT (CAP); filgotinib - JYSELECA (CAP); tofacitinib - XELJANZ (CAP); upadacitinib - RINVOQ (CAP) – EMEA/H/A-20/1517

AbbVie Deutschland GmbH & Co. KG (Rinvoq), Eli Lilly Nederland B.V. (Olumiant), Galapagos N.V. (Jyseleca), Pfizer Europe MA EEIG (Cibinqo, Xeljanz)

Referral PRAC Rapporteur: Ulla Wändel Liminga; Referral PRAC Co-rapporteur(s): Liana

[1] Indicated for the treatment of inflammatory disorders

Gross-Martirosyan (Olumiant, Xeljanz), Nikica Mirošević Skvrce (Cibinqo, Jyseleca, Rinvoq)

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

Revised opinion; the PRAC adopted a revised recommendation to CHMP at their January 2023 meeting.

Action: For adoption

The CHMP noted the revised PRAC recommendation.

The CHMP adopted a revised opinion by majority (24 out of 30 votes), recommending that the marketing authorisations for Cibinqo, Jyseleca, Olumiant, Rinvoq and Xeljanz should be varied.

The divergent position (Margareta Bego, Ondrej Slanar, Alexandre Moreau, Armando Genazzani, Johann Lodewijk Hillege, Blanka Hirschlerova) was appended to the opinion.

The CHMP agreed to the DHPC and communication plan.

The public health communication was circulated for information.

10.1.2. Adakveo - crizanlizumab - Orphan - EMEA/H/C/004874

Novartis Europharm Limited

Referral Rapporteur: Daniela Philadelphy, Referral Co-Rapporteur: Johanna Lähteenvuo

Scope: The European Commission (EC) initiated a procedure under Article 20 of Regulation (EC) No 726/2004 and requested the Agency/CHMP to assess the benefit-risk balance of the centrally authorised medicinal product Adakveo (crizanlizumab) in its approved indication. In addition, the EC requested the Agency/CHMP to consider as soon as possible whether temporary measures were necessary to protect public health.

The initiation of the review follows preliminary results from the Phase III study (CSEG101A2301, STAND) which is a specific obligation to the conditional marketing authorisation for Adakveo. The preliminary results for STAND study show no superiority of crizanlizumab over placebo in annualised rates of vaso-occlusive crises leading to a healthcare visit over the first-year post randomisation.

Action: For adoption

See 9.1

The CHMP appointed Daniela Philadelphy as Referral Rapporteur and Johanna Lähteenvuo as Referral Co-Rapporteur.

The CHMP considered the need for temporary measures to ensure the safe and effective use of this medicinal product while the review is ongoing. The CHMP considered at this point that a detailed assessment of further data on STAND study, in the context of all available data on Adavkeo was necessary, before making recommendations on its authorised use. The CHMP considered however, that the preliminary results available should be communicated to healthcare professional, and adopted the content of a DHPC, together with a communication plan to this effect.

The CHMP adopted a list of questions with a procedural timetable.

Notification: 26.01.2023

Start of the procedure (CHMP): January 2023 CHMP

List of questions: 26.01.2023

Submission of responses: 01.03.2023

Re-start of the procedure: 22.03.2023

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 05.04.2023

Comments: 13.04.2023

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 19.04.2023

CHMP list of outstanding issues or CHMP Opinion: April 2023 CHMP

10.2. Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004

10.2.1. Colistimethate sodium (CMS) – EMEA/H/A-5(3)/1524

Various MAHs

Referral Rapporteur: Martina Weise, Referral Co-Rapporteur: Ewa Balkowiec Iskra

Scope: Start of procedure, appointment of rapporteurs

Review of the ratio of polymyxins E1 and E2 in colistin starting material and of the (sulfomethylation) composition profile of CMS finished product.

Action: For adoption

The CHMP appointed Martina Weise as referral Rapporteur and Ewa Balkowiec Iskra as referral Co-Rapporteur.

The CHMP adopted the procedural timetable.

Notification: 20.01.2023

Start of the procedure (CHMP): January 2023 CHMP

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 02.05.2023

Comments: 08.05.2023

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 11.05.2023

CHMP list of questions/opinion: May 2023 CHMP

10.3. Procedure under Articles 5(2) and 10 of Regulation (EC) No 726/2004

No items

10.4. Disagreement between Member States on application for medicinal product (potential serious risk to public health) –under Article 29(4) of Directive 2001/83/EC

No items

10.5. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC

No items

10.6. Community Interests - Referral under Article 31 of Directive 2001/83/EC

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

Applicant(s): various

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

Scope: List of questions (LoQ) for the SAG Neurology adopted by the PRAC on 12.01.2023

Action: For endorsement

The CHMP endorsed the list of questions for the SAG Neurology adopted by the PRAC on 12.01.2023.

10.7. Re-examination Procedure under Article 32(4) of Directive 2001/83/EC

No items

10.8. Procedure under Article 107(2) of Directive 2001/83/EC

No items

10.9. Disagreement between Member States on Type II variation– Arbitration procedure initiated by MAH under Article 6(13) of Commission Regulation (EC) No 1084/2003

No items

10.10. Procedure under Article 29 of Regulation (EC) 1901/2006

No items

10.11. Referral under Article 13 Disagreement between Member States on Type II variation– Arbitration procedure initiated by Member State under Article 13 (EC) of Commission Regulation No 1234/2008

No items

11. Pharmacovigilance issue

11.1. Early Notification System

January 2023 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

The CHMP noted the information.

12. Inspections

12.1. GMP inspections

Information related to GMP inspections will not be published as it undermines the purpose of such inspections.

12.2. GCP inspections

Information related to GCP inspections will not be published as it undermines the purpose of such inspections.

12.3. Pharmacovigilance inspections

Information related to Pharmacovigilance inspections will not be published as it undermines the purpose of such inspections.

12.4. GLP inspections

Information related to GLP inspections will not be published as it undermines the purpose of such inspections.

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

No items

13.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Vote by proxy

No topics

14.1.2. CHMP membership

New membership:

The Chair welcomed Beata Maria Jakline-Ullrich, as the new alternate for Hungary and Christian Gartner, as the new alternate for Austria.

CHMP co-opted membership

With his nomination as CHMP alternate for Austria, the co-opted member mandate for Christian Gartner came to an end on 31.12.2022. CHMP decided at the January 2023 PROM that the co-opted member position should be filled in again. Members were asked to send proposals for the area(s) of expertise.

Action: For discussion

The CHMP agreed that a co-opted member should be appointed in the following area of expertise: biostatistics/ clinical trial methodology.

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for January 2023

Action: For adoption

The CHMP adopted the EURD list.

14.2.2. Paediatric Committee (PDCO)

PIPs reaching D30 at January 2023 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 17-20 January 2023

Action: For information

The CHMP noted the information.

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/ Sean Barry

Reports from BWP January 2023 meeting to CHMP for adoption:

- 10 reports on products in scientific advice and protocol assistance
- 6 reports on products in pre-authorisation procedures
- 5 reports on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports.

14.3.2. Scientific Advice Working Party (SAWP)

Chair: Paolo Foggi

Report from the SAWP meeting held on 09-12 January 2023. Table of conclusions

Action: For information

Scientific advice letters:

Information related to scientific advice letters cannot be released at present time as these contain commercially confidential information.

The CHMP noted the update.

14.3.3. Quality Working Party (QWP)

Election of Quality Working Party chair. QWP Chair Blanka Hirschlerova's first term will expire in February 2023. A call for nomination of a QWP chair was launched during the December 2022 PROM meeting.

Nomination(s) received

Action: For election

The CHMP re-elected Blanka Hirschlerova as chair of the Quality Working Party.

14.3.4. Rheumatology and Immunology Working Party (RIWP)

Election of Rheumatology and Immunology Working Party chair. A call for nomination of a RIWP chair was launched during the December 2022 PROM meeting.

Nomination(s) received

Action: For election

The CHMP elected Caroline Auriche Benichou as chair of the Rheumatology and Immunology Working Party.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

14.6. Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

The CHMP noted the information.

15.1.2. COVID-19 vaccine - EMEA/H/C/006058

immunisation to prevent COVID-19 caused by SARS-CoV-2

Scope: rolling review, list of questions

Action: For adoption

The Committee discussed the issues identified in this application, relating to quality and clinical aspects.

The Committee adopted a request for supplementary information.

Lists of participants

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 23-26 January 2023 CHMP meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Harald Enzmann	Chair	Germany	No interests declared	
Daniela Philadelphy	Member	Austria	No interests declared	
Christian Gartner	Alternate	Austria	No interests declared	
Christophe Focke	Member	Belgium	No restrictions applicable to this meeting	
Karin Janssen van Doorn	Alternate	Belgium	No interests declared	
Ilko Getov	Member	Bulgaria	No interests declared	
Margareta Bego	Member	Croatia	No interests declared	
Selma Arapovic Dzakula	Alternate	Croatia	No interests declared	
Helena Panayiotopoulou	Member	Cyprus	No interests declared	
Emilia Mavrokordatou	Alternate	Cyprus	No participation in final deliberations and voting on:	COVID-19 vaccines
Ondřej Slanař	Member	Czechia	No restrictions applicable to this meeting	
Tomas Radimersky	Alternate	Czechia	No interests declared	
Thalia Marie Estrup Blicher	Member	Denmark	No interests declared	
Aaron Sosa Mejia	Alternate	Denmark	No participation in final deliberations and voting on:	Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/X/0016
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Edward Laane	Alternate	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Johanna Lähteenvuo	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Martina Weise	Member	Germany	No restrictions applicable to this meeting	
Janet Koenig	Alternate	Germany	No interests declared	
Konstantina Alexopoulou	Member	Greece	No interests declared	
Anastasia Mountaki	Alternate	Greece	No interests declared	
Robert Porszasz	Member	Hungary	No interests declared	
Beata Maria Jakline Ullrich	Alternate	Hungary	No interests declared	
Hjalti Kristinsson	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Finbarr Leacy	Alternate	Ireland	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Armando Genazzani	Member	Italy	No interests declared	
Maria Grazia Evandri	Alternate	Italy	No interests declared	
Elita Poplavska	Member	Latvia	No interests declared	
Vilma Petrikaite	Member	Lithuania	No interests declared	
Martine Trauffler	Member	Luxembourg	No interests declared	
Alexandra Branchu	Alternate	Luxembourg	No participation in discussion, final deliberations and voting on:	Dupixent - dupilumab - EMEA/H/C/004390/II/0060
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Ingrid Wang	Member	Norway	No interests declared	
Eva Skovlund	Alternate	Norway	No interests declared	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Member (Vice-Chair)	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No participation in final deliberations and voting on:	COVID-19 vaccines
Simona Badoi	Member	Romania	No interests declared	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Dorota Distlerova	Alternate	Slovakia	No interests declared	
Kristina Nadrah	Member	Slovenia	No restrictions applicable to this meeting	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Blanca Garcia-Ochoa	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Carla Torre	Co-opted member	Portugal	No interests declared	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Blanka Hirschlerova	Co-opted member	Czechia	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Martijn van Gils	Expert	Netherlands	No interests declared	
Carla Herberts	Expert	Netherlands	No interests declared	
Paolo Foggi	Expert	Italy	No interests declared	
Peter Mol	Expert	Netherlands	No interests declared	
Dina Apele-Freimane	Expert	Latvia	No restrictions applicable to this meeting	
Elina Rönnemaa	Expert	Sweden	No interests declared	
Elmer Schabel	Expert	Germany	No interests declared	
Leon van Aerts	Expert	Netherlands	No interests declared	
Kairi Rooma	Expert	Estonia	No interests declared	
Ulla Wändel Liminga	Expert	Sweden	No interests declared	
Martin Huber	Expert	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jelena Katic	Expert	Germany	No interests declared	
Tania Meier	Expert	Germany	No interests declared	
Caroline Auriche-Benichou	Expert	France	No interests declared	
Danica Juricic Nahal	Expert	Croatia	No interests declared	
Paula Contreras Alarcón	Expert	Spain	No participation in discussion, final deliberations and voting on:	Rinvoq - upadacitinib - EMEA/H/C/004760/II/0027 Janus kinase (JAK) inhibitors - EMEA/H/A-20/1517
Maria del Pilar Rayon	Expert	Spain	No interests declared	
Consuelo Mejías Pavón	Expert	Spain	No interests declared	
Maria Martinez Gonzalez	Expert	Spain	No interests declared	
Alicia Pérez González	Expert	Spain	No interests declared	
Vincent Gazin	Expert	France	No interests declared	
Celine Jumeau	Expert	France	No interests declared	
Roxane Fornacciari	Expert	France	No interests declared	
Bruno Delafont	Expert	France	No participation in discussion, final deliberations and voting on:	Lynparza - olaparib - EMEA/H/C/003726/II/0058
Sargi Caizergues Lama	Expert	France	No interests declared	
Ismail Rafik	Expert	France	No interests declared	
Nicolas Beix	Expert	France	No interests declared	
Nina Hessvik	Expert	Norway	No interests declared	
Anne-Berit Erdal	Expert	Norway	No interests declared	
Jens Peter Hartmann	Expert	Germany	No interests declared	
Katharina Hees	Expert	Germany	No interests declared	
Claudia Reichmann	Expert	Germany	No interests declared	
Jörg Engelbergs	Expert	Germany	No interests declared	
Hilke Zander	Expert	Germany	No interests declared	
Sara Tognarelli	Expert	Germany	No restrictions applicable to this meeting	
Quirine Fillekes	Expert	Netherlands	No interests declared	
Liesbeth Van Vlijmen	Expert	Netherlands	No interests declared	
Loes den Otter	Expert	Netherlands	No interests declared	
Ate Duursma	Expert	Netherlands	No interests declared	
Valentina Lorenzi	Expert	Netherlands	No interests declared	
Kommerie Hendrik	Expert	Netherlands	No interests declared	
Andre Elferink	Expert	Netherlands	No interests declared	
Cristel Loeb	Expert	Netherlands	No interests declared	
Esther Brandon	Expert	Netherlands	No interests declared	
Jaap Fransen	Expert	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Elly Vereyken	Expert	Netherlands	No restrictions applicable to this meeting	
Marjolijn Schalk	Expert	Netherlands	No interests declared	
Charlotte de Wolf	Expert	Netherlands	No interests declared	
Angela de Kleynen	Expert	Netherlands	No interests declared	
Chiara Acone	Expert	Netherlands	No restrictions applicable to this meeting	
Jan Welink	Expert	Netherlands	No interests declared	
Ebru Karakoc Madsen	Expert	Denmark	No restrictions applicable to this meeting	
Emilie Birch Kristensen	Expert	Denmark	No restrictions applicable to this meeting	
Line Praest Lauridsen	Expert	Denmark	No restrictions applicable to this meeting	
Thadeus Bao Quan Nguyen	Expert	Denmark	No interests declared	
Kristina Bech Jensen	Expert	Denmark	No interests declared	
Charlotte Hejl	Expert	Denmark	No restrictions applicable to this meeting	
Deirdre Mannion	Expert	Denmark	No restrictions applicable to this meeting	
Nanna Borup Johansen	Expert	Denmark	No interests declared	
Sine Buhl Naess-Schmidt	Expert	Denmark	No restrictions applicable to this meeting	
Torsten Holm Nielsen	Expert	Denmark	No restrictions applicable to this meeting	
Marianne Løiten Dalhus	Expert	Norway	No interests declared	
Fabrice Eroukhmanoff	Expert	Norway	No interests declared	
Ingrid Lund	Expert	Norway	No interests declared	
Veronica Krogstad	Expert	Norway	No interests declared	
Agnieszka Przybyszewska	Expert	Ireland	No interests declared	
Benita Cullen	Expert	Ireland	No interests declared	
Sinead Harrington	Expert	Ireland	No interests declared	
Angelo Molinaro	Expert	Italy	No interests declared	
Salvatore Tranchina	Expert	Italy	No interests declared	
Antonella Isgrò	Expert	Italy	No interests declared	
Angela Garau	Expert	Italy	No interests declared	
Adriana Ammassari	Expert	Italy	No interests declared	
Luca Santi	Expert	Italy	No restrictions applicable to this meeting	
Martina Perini	Expert	Italy	No participation in discussion, final deliberations and voting on:	pegunigalsidase alfa - Orphan - EMEA/H/C/005618
Giancarlo Zito	Expert	Italy	No interests declared	
Susanna Hausmann	Expert	Germany	No interests declared	
Julian Paesler	Expert	Germany	No interests declared	
Michael Schramm	Expert	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Karl Katholnig	Expert	Austria	No restrictions applicable to this meeting	
Philipp Janesch	Expert	Austria	No interests declared	
Susanne Urach	Expert	Austria	No interests declared	
Angelina Doriguzzi	Expert	Austria	No restrictions applicable to this meeting	
Elisabeth Wischnitzki	Expert	Austria	No interests declared	
Walter Johannes Beiersdorf	Expert	Austria	No restrictions applicable to this meeting	
Femke Geers	Expert	Netherlands	No interests declared	
Torunn Lisbeth Wangen	Expert	Norway	No interests declared	
Albena Mihailova	Expert	Norway	No interests declared	
Valerie Lescrainier	Expert	Belgium	No interests declared	
Olga Kholmanskikh	Expert	Belgium	No interests declared	
Violette Dirix	Expert	Belgium	No interests declared	
Karin Fjordén	Expert	Sweden	No restrictions applicable to this meeting	
Jenny-Maria Jönsson	Expert	Sweden	No participation in final deliberations and voting on:	Rubraca - rucaparib - EMEA/H/C/004272/II/0037 Lynparza - olaparib - EMEA/H/C/003726/II/0058
Maria Linnea Asp	Expert	Sweden	No restrictions applicable to this meeting	
Per Hagstam	Expert	Sweden	No interests declared	
Emmely de Vries	Expert	Netherlands	No interests declared	
Gaetan Philippot	Expert	Netherlands	No interests declared	
Meera Varma	Expert	Denmark	No restrictions applicable to this meeting	
Theis Moeslund Jensen	Expert	Denmark	No restrictions applicable to this meeting	
Sabine Mayrhofer	Expert	Germany	No interests declared	
Nora Cascante Estepa	Expert	Germany	No interests declared	
Maria Victoria Tudanca Pacios	Expert	Spain	No restrictions applicable to this meeting	
A representative from the European Commission attended the meeting				
Meeting run with the help of EMA staff				

Experts were evaluated against the agenda topics or activities they participated in.

Experts from international organisations or regulatory authorities in third countries cannot participate in the adoption of any procedural decision, scientific opinion or recommendation by the Committee at any step of the procedure.

Explanatory notes

The notes below give a brief explanation of the main sections and headings in the CHMP agenda and should be read in conjunction with the agenda or the minutes.

Oral explanations *(section 2)*

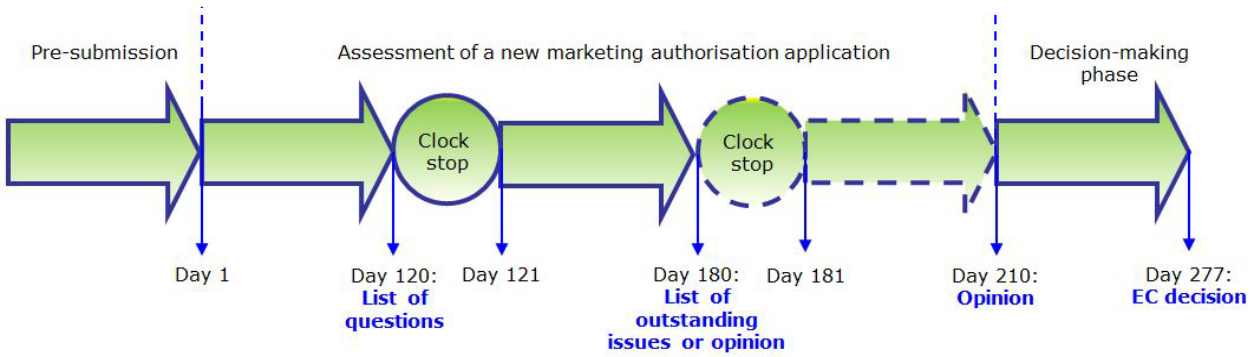
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (section 10) but can relate to any other issue for which the CHMP would like to discuss with company representatives in person.

Initial applications *(section 3)*

This section lists applications for marketing authorisations of new medicines that are to be discussed by the Committee.

Section 3.1 is for medicinal products nearing the end of the evaluation and for which the CHMP is expected to adopt an **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CHMP. The clock stop happens after day 120 and may also happen after day 180, when the CHMP has adopted a list of questions or outstanding issues to be addressed by the company. Related discussions are listed in the agenda under sections 3.2 (**Day 180 List of outstanding issues**) and 3.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 3.4, **update on ongoing new applications for centralised procedures**.

The assessment leads to an opinion from the CHMP by day 210. Following a CHMP opinion the European Commission takes usually 67 days to issue a legally binding decision (i.e. by day 277 of the procedure). CHMP discussions on products that have received a CHMP opinion and are awaiting a decision are listed under section 3.6, **products in the decision making phase**.

Extension of marketing authorisations according to Annex I of Reg. 1234/2008 *(section 4)*

Extensions of marketing authorisations are applications for the change or addition of new strengths, formulations or routes of administration to existing marketing authorisations. Extension applications follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

Type II variations - Extension of indication procedures *(section 5)*

Type II variations are applications for a change to the marketing authorisation which requires an update of the product information and which is not covered in section 4. Type II variations include applications for a new use of the medicine (extension of indication), for which the assessment takes up to 90 days. For the applications listed in this section, the CHMP may adopt an opinion or request supplementary information from the applicant.

Ancillary medicinal substances in medical devices *(section 6)*

Although the EMA does not regulate medical devices it can be asked by the relevant authorities (the so-called Notified Bodies) that are responsible for regulating these devices to give a scientific opinion on a medicinal substance contained in a medical device.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 *(section 3.5)*

This section lists applications for new marketing authorisation for which the applicant has requested a re-examination of the opinion previously issued by the CHMP.

Re-examination procedures *(section5.3)*

This section lists applications for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP.

Withdrawal of application *(section 3.7)*

Applicants may decide to withdraw applications at any stage during the assessment and a CHMP opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use) *(section 7)*

Compassionate use is a way of making available to patients with an unmet medical need a promising medicine which has not yet been authorised (licensed) for their condition. Upon request, the CHMP provides recommendations to all EU Member States on how to administer, distribute and use certain medicines for compassionate use.

Pre-submission issues *(section 8)*

In some cases the CHMP may discuss a medicine before a formal application for marketing authorisation is submitted. These cases generally refer to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation. In case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

Post-authorisation issues *(section 9)*

This section lists other issues concerning authorised medicines that are not covered elsewhere in the agenda. Issues include supply shortages, quality defects, some annual reassessments or renewals or type II variations to marketing authorisations that would require specific discussion at the plenary.

Referral procedures *(section 10)*

This section lists referrals that are ongoing or due to be started at the plenary meeting. 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 EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 11)*

This section lists issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines. Feedback is provided by the PRAC. This section also refers to the early notification system, a system used to notify the European regulatory network on proposed EMA communication on safety of medicines.

Inspections Issues *(section 12)*

This section lists inspections that are undertaken for some medicinal products. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Innovation task force *(section 13)*

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes from the last ITF meeting as well as any related issue that requires discussion with the CHMP are listed in this section of the agenda. Further information on the ITF can be found here.

Scientific advice working party (SAWP) *(section 14.3.1)*

This section refers to the monthly report from the CHMP's Scientific Advice Working Party (SAWP) on scientific advice given to companies during the development of medicines. Further general information on SAWP can be found here.

Satellite groups / other committees *(section 14.2)*

This section refers to the reports from groups and committees making decisions relating to human medicines: the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), the Committee for Orphan Medicinal Products (COMP), the Committee for Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmamacovigilance Risk Assessment Committee (PRAC).

Invented name issues *(section 14.3)*

This section list issues related to invented names proposed by applicants for new medicines. The CHMP has established the Name Review Group (NRG) to perform reviews of the invented names. The group's main role is to consider whether the proposed names could create a public-health concern or potential safety risk. Further information can be found here.

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 April 2023
EMA/CHMP/44601/2023

Annex to 23-26 January 2023 CHMP Minutes

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for January 2023: **For adoption**	Adopted

A.2. Appointment of Rapporteur / Co-Rapporteur Full Applications

Final Outcome of Rapporteurship allocation for January 2023: **For adoption**	Adopted

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

Information related to pre-submission of initial applications cannot be released at the present time as these contain commercially confidential information.

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

B.1.1. Annual reassessment for products authorised under exceptional circumstances

Myalepta - metreleptin - EMEA/H/C/004218/S/0030, Orphan Amryt Pharmaceuticals DAC, Rapporteur: Karin Janssen van Doorn, Co-Rapporteur: Robert Porszasz, PRAC Rapporteur: Adam Przybylkowski	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

B.2.1. Renewals of Marketing Authorisations requiring 2nd Renewal

Myalepta - metreleptin - EMEA/H/C/004218/R/0031, Orphan Amryt Pharmaceuticals DAC, Rapporteur: Karin Janssen van Doorn, Co-Rapporteur: Robert Porszasz, PRAC Rapporteur: Adam Przybylkowski	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that an additional five-year renewal was required.
Verkazia - ciclosporin - EMEA/H/C/004411/R/0021, Orphan Santen Oy, Duplicate, Duplicate of IKERVIS,	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

Rapporteur: Jayne Crowe, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Jan Neuhauser	Based on the review of the available information, the CHMP was of the opinion that an additional five-year renewal was required.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

BLINCYTO - blinatumomab - EMEA/H/C/003731/R/0048, Orphan Amgen Europe B.V., Rapporteur: Alexandre Moreau, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Eva Jirsová	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.
Carmustine Obvius - carmustine - EMEA/H/C/004326/R/0009 Obvius Investment B.V, Generic, Rapporteur: Elita Poplavska, PRAC Rapporteur: Jan Neuhauser Request for Supplementary Information adopted on 15.12.2022.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.
Dzuveo - sufentanil - EMEA/H/C/004335/R/0009 Laboratoire Aguettant, Rapporteur: Hrefna Gudmundsdottir, PRAC Rapporteur: Adam Przybylkowski	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.
Lojuxta - lomitapide - EMEA/H/C/002578/R/0054 Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Lonquex - lipegfilgrastim - EMEA/H/C/002556/R/0077 Teva B.V., Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kirsti Villikka Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Nerlynx - neratinib - EMEA/H/C/004030/R/0031 Pierre Fabre Medicament, Rapporteur: Bruno Sepodes, Co-Rapporteur: Alexandre Moreau,	Request for supplementary information adopted with a specific timetable.

PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 26.01.2023.	
Nityr - nitisinone - EMEA/H/C/004582/R/0015 Cycle Pharmaceuticals (Europe) Limited, Generic, Generic of Orfadin, Rapporteur: Jayne Crowe, PRAC Rapporteur: Amelia Cupelli Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Prasugrel Mylan - prasugrel - EMEA/H/C/004644/R/0014 Mylan Pharmaceuticals Limited, Generic, Generic of Efient, Rapporteur: Alar Irs, PRAC Rapporteur: Anette Kirstine Stark Request for Supplementary Information adopted on 10.11.2022.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.
RXULTI - brexpiprazole - EMEA/H/C/003841/R/0014 Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Armando Genazzani, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Lucia Kuráková Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Tegsedi - inotersen - EMEA/H/C/004782/R/0035, Orphan Akcea Therapeutics Ireland Limited, Rapporteur: Martina Weise, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Rhea Fitzgerald	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.
Trazimera - trastuzumab - EMEA/H/C/004463/R/0020 Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Sol Ruiz, PRAC Rapporteur: Brigitte Keller-Stanislawski	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.

B.2.3. Renewals of Conditional Marketing Authorisations

CARVYKTI - ciltacabtagene autoleucel - EMEA/H/C/005095/R/0008, Orphan, ATMP Janssen-Cilag International NV, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Marcos	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal

Timón, CHMP Coordinators: Jan Mueller-Berghaus and Blanca Garcia-Ochoa, PRAC Rapporteur: Jo Robays	for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional.
Deltyba - delamanid - EMEA/H/C/002552/R/0062, Orphan Otsuka Novel Products GmbH, Rapporteur: Christophe Focke, PRAC Rapporteur: Jo Robays Request for Supplementary Information adopted on 15.12.2022.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional.
Lorviqua - lorlatinib - EMEA/H/C/004646/R/0025 Pfizer Europe MA EEIG, Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Nikica Mirošević Skvrce	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional.
Ondexxya - andexanet alfa - EMEA/H/C/004108/R/0034 AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (h5n1) (live attenuated, nasal) - EMEA/H/C/003963/R/0057 AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik	Positive Opinion adopted by consensus together with the CHMP assessment report. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional.
WAYLIVRA - volanesorsen - EMEA/H/C/004538/R/0022, Orphan Akcea Therapeutics Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Martin Huber Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection	
PRAC recommendations on signals adopted at the PRAC meeting held on 09-12 January 2023 PRAC:	
Signal of myasthenia gravis Pravafenix / Cholib - 3-hydroxy 3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins): atorvastatin; fluvastatin; lovastatin; pitavastatin; pravastatin; rosuvastatin; simvastatin and other relevant fixed dose combinations; pravastatin, fenofibrate; simvastatin, fenofibrate Rapporteurs: multiple, Co-Rapporteurs: multiple, PRAC Rapporteur: Nathalie Gault PRAC recommendation on a variation **Action:** For adoption	Adopted
Signal of haemophagocytic lymphohistiocytosis (HLH) Tafinlar / Mekinist - Dabrafenib; trametinib Rapporteurs: multiple, Co-Rapporteurs: multiple, PRAC Rapporteur: Ulla Wändel Liminga PRAC recommendation on a variation **Action:** For adoption	Adopted
Signal of thrombotic microangiopathy Stivarga - Regorafenib Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst PRAC recommendation on a variation **Action:** For adoption	Adopted
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its January 2023 meeting:	

EMEA/H/C/PSUSA/00000209/202205 (anakinra) CAPS: **Kineret** (EMEA/H/C/000363) (anakinra), Swedish Orphan Biovitrum AB (publ), Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Anette Kirstine Stark, "01/05/2019 To: 01/05/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to remove a warning/precaution regarding the risk of MAS in patients with Still's disease. The Package leaflet is updated accordingly. An editorial change to section 5.1 of the SmPC was also included.
EMEA/H/C/PSUSA/00010389/202206 (human papillomavirus 9-valent vaccine (recombinant, adsorbed)) CAPS: **Gardasil 9** (EMEA/H/C/003852) (human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed)), Merck Sharp & Dohme B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Jean-Michel Dogné, "09/06/2021 To: 09/06/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above-mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to remove the sentence that refers to the possibility of observing the same adverse events for Gardasil and Gardasil 9.
EMEA/H/C/PSUSA/00010671/202205 (semaglutide) CAPS: **Ozempic** (EMEA/H/C/004174) (semaglutide), Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege **Rybelsus** (EMEA/H/C/004953) (semaglutide), Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege **Wegovy** (EMEA/H/C/005422) (semaglutide), Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Mari Thorn, "01/06/2021 To: 31/05/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC of oral semaglutide (Rybelsus) to add the adverse reaction dysgeusia with a frequency "uncommon". The package leaflet is updated accordingly. Update of section 4.8 of the SmPC of semaglutide (Ozempic, Rybelsus and Wegovy) to add the adverse reaction delayed gastric emptying with a frequency "uncommon". The package leaflet is updated accordingly.

EMEA/H/C/PSUSA/00010761/202205 (pegvaliase) CAPS: **Palynziq** (EMEA/H/C/004744) (pegvaliase), BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "24/05/2021 To: 23/05/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add the adverse reactions diarrhoea and fatigue with a frequency of very common. The package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00010912/202206 (COVID-19 Vaccine (ChAdOx1-S [recombinant]) (Vaxzevria)) CAPS: **Vaxzevria** (EMEA/H/C/005675) (COVID 19 vaccine (ChAdOx1 S [recombinant])), AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, "29/12/2021 To: 28/06/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above-mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add cutaneous vasculitis with a frequency 'not known'. The package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00010942/202205 (relugolix / estradiol / norethisterone acetate) CAPS: **Ryeqo** (EMEA/H/C/005267) (relugolix / estradiol / norethisterone acetate), Gedeon Richter Plc., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "25/11/2021 To: 25/05/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add urticaria and angioedema as adverse drug reactions with a frequency 'uncommon'. The package leaflet is updated accordingly.

B.4. EPARs / WPARs

Dimethyl fumarate Accord - dimethyl fumarate - EMEA/H/C/005950 Accord Healthcare S.L.U., treatment of multiple sclerosis, Generic, Generic of TECFIDERA, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Spevigo - spesolimab - EMEA/H/C/005874	For information only. Comments can be sent to

Boehringer Ingelheim International GmbH; treatment of flares in adult patients with generalised pustular psoriasis New active substance (Article 8(3) of Directive No 2001/83/EC)	the PL in case necessary.
Hemgenix - etranacogene dezaparvovec - EMEA/H/C/004827, Orphan, ATMP CSL Behring GmbH, treatment of adults with Haemophilia B, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
IMJUDO - tremelimumab - EMEA/H/C/006016 AstraZeneca AB, For use in combination with durvalumab for the treatment of adults with unresectable hepatocellular carcinoma., New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
OMBLASTYS - iodine (131I) omburtamab - EMEA/H/C/005499, Orphan Y-Mabs Therapeutics A/S, treatment of neuroblastoma, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Pombiliti - cipaglucosidase alfa - EMEA/H/C/005703, Orphan Amicus Therapeutics Europe Limited, treatment of adults aged 18 years and older with Pompe disease, Known active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Tremelimumab AstraZeneca - tremelimumab - EMEA/H/C/004650 AstraZeneca AB, treatment of adults with metastatic NSCLC with no sensitising epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumour aberrations, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

Scopes related to Chemistry, Manufacturing, and Controls cannot be released at the present time as these contain commercially confidential information.

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Adjupanrix - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/II/0081/G	Request for supplementary information adopted with a specific timetable.

GlaxoSmithkline Biologicals SA, Informed Consent of Pandemrix (EXP), Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 19.01.2023.	
Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0046/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
Aybintio - bevacizumab - EMEA/H/C/005106/II/0016 Samsung Bioepis NL B.V., Rapporteur: Christian GartnerRequest for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Benepali - etanercept - EMEA/H/C/004007/II/0069 Samsung Bioepis NL B.V., Rapporteur: Christian Gartner Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
Besremi - ropeginterferon alfa-2b - EMEA/H/C/004128/II/0026 AOP Orphan Pharmaceuticals GmbH, Rapporteur: Janet Koenig Opinion adopted on 19.01.2023. Request for Supplementary Information adopted on 08.12.2022.	Positive Opinion adopted by consensus on 19.01.2023.
CEVENFACTA - eptacog beta (activated) - EMEA/H/C/005655/II/0002 Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Daniela Philadelphy Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0159/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
Cosentyx - secukinumab - EMEA/H/C/003729/II/0095/G Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola Opinion adopted on 19.01.2023.	Positive Opinion adopted by consensus on 19.01.2023.
Cosentyx - secukinumab -	Request for supplementary information adopted

EMEA/H/C/003729/II/0096 Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 19.01.2023.	with a specific timetable.
Defitelio - defibrotide - EMEA/H/C/002393/II/0059, Orphan Gentium S.r.l., Rapporteur: Kristina Dunder Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 17.11.2022.	Positive Opinion adopted by consensus on 12.01.2023.
Flixabi - infliximab - EMEA/H/C/004020/II/0077/G Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
Grepid - clopidogrel - EMEA/H/C/001059/II/0054 Pharmathen S.A., Generic, Generic of Plavix, Rapporteur: Nevenka Trsinar Brodt Request for Supplementary Information adopted on 26.01.2023, 15.09.2022.	Request for supplementary information adopted with a specific timetable.
Hemlibra - emicizumab - EMEA/H/C/004406/II/0033 Roche Registration GmbH, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Humira - adalimumab - EMEA/H/C/000481/II/0215 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
Idefirix - imlifidase - EMEA/H/C/004849/II/0010, Orphan Hansa Biopharma AB, Rapporteur: Martina Weise Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
IMVANEX - smallpox vaccine (live modified vaccinia virus Ankara) - EMEA/H/C/002596/II/0079 Bavarian Nordic A/S, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 26.01.2023. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 26.01.2023.

on 27.10.2022.	
Ivabradine Zentiva - ivabradine - EMEA/H/C/004117/II/0014 Zentiva k.s., Generic, Generic of Procoralan, Rapporteur: Tomas Radimersky Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Kovaltry - octocog alfa - EMEA/H/C/003825/II/0040/G Bayer AG, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
LifeGlobal Media - human albumin solution - EMEA/H/D/004287/II/0005/G LifeGlobal Group LLC, Rapporteur: Maria Grazia Evandri Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0025 Les Laboratoires Servier, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0039, Orphan Advanced Accelerator Applications, Rapporteur: Janet Koenig Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Menveo - meningococcal group a, c, w135 and y conjugate vaccine - EMEA/H/C/001095/II/0115/G GSK Vaccines S.r.l, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0047/G, Orphan Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.
NUVAXOVID - NVX-CoV2373 - EMEA/H/C/005808/II/0035/G Novavax CZ, a.s., Rapporteur: Johann Lodewijk	Request for supplementary information adopted with a specific timetable.

Hillege Request for Supplementary Information adopted on 12.01.2023.	
NUVAXOVID - NVX-CoV2373 - EMEA/H/C/005808/II/0039/G Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0035/G Roche Registration GmbH, Rapporteur: Thalia Marie Estrup Blicher Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Padcev - enfortumab vedotin - EMEA/H/C/005392/II/0006/G Astellas Pharma Europe B.V., Rapporteur: Aaron Sosa Mejia Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.
Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0019/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 13.10.2022.	Positive Opinion adopted by consensus on 26.01.2023. See 9.1
Replagal - agalsidase alfa - EMEA/H/C/000369/II/0122 Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Rotarix - rotavirus vaccine (live, oral) - EMEA/H/C/000639/II/0128 GlaxoSmithKline Biologicals S.A., Rapporteur: Christophe Focke Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
Rybelsus - semaglutide - EMEA/H/C/004953/II/0030 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
Somavert - pegvisomant - EMEA/H/C/000409/II/0104	Positive Opinion adopted by consensus on 26.01.2023.

Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 15.12.2022, 10.11.2022.	
Surgiflo Haemostatic Matrix Kit - human thrombin - EMEA/H/D/002301/II/0032/G Ferrosan Medical Devices A/S, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
TEZSPIRE - tezepelumab - EMEA/H/C/005588/II/0001 AstraZeneca AB, Rapporteur: Finbarr Leacy, PRAC Rapporteur: Eva Jirsová Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 01.12.2022.	Positive Opinion adopted by consensus on 12.01.2023.
Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0039, Orphan BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 27.10.2022.	Positive Opinion adopted by consensus on 12.01.2023.
Vydura - rimegepant - EMEA/H/C/005725/II/0002/G Pfizer Europe MA EEIG, Rapporteur: Janet Koenig Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 20.10.2022.	Positive Opinion adopted by consensus on 12.01.2023.
Xofigo - radium-223 - EMEA/H/C/002653/II/0047 Bayer AG, Rapporteur: Janet Koenig Opinion adopted on 19.01.2023. Request for Supplementary Information adopted on 10.11.2022.	Positive Opinion adopted by consensus on 19.01.2023.
Zercepac - trastuzumab - EMEA/H/C/005209/II/0022 Accord Healthcare S.L.U., Rapporteur: Sol Ruiz Opinion adopted on 19.01.2023.	Positive Opinion adopted by consensus on 19.01.2023.
ZYNRELEF - bupivacaine / meloxicam - EMEA/H/C/005205/II/0009/G Heron Therapeutics, B.V., Rapporteur: Alexandre Moreau Opinion adopted on 12.01.2023. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 12.01.2023.

on 22.09.2022.	
WS2344 **Ryzodeg-** **EMEA/H/C/002499/WS2344/0048** **Tresiba-EMEA/H/C/002498/WS2344/0056** **Xultophy-** **EMEA/H/C/002647/WS2344/0044** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 01.12.2022, 27.10.2022.	Positive Opinion adopted by consensus on 12.01.2023.
WS2362 **Edistride-** **EMEA/H/C/004161/WS2362/0057** **Forxiga-** **EMEA/H/C/002322/WS2362/0078** AstraZeneca AB, Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
WS2388/G **Fluenz Tetra-** **EMEA/H/C/002617/WS2388/0122/G** **Pandemic influenza vaccine H5N1 AstraZeneca-** **EMEA/H/C/003963/WS2388/0056/G** AstraZeneca AB, Lead Rapporteur: Christophe Focke Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.
WS2394 **Hexacima-** **EMEA/H/C/002702/WS2394/0141** **Hexyon-** **EMEA/H/C/002796/WS2394/0145** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.

B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects

Beyfortus - nirsevimab - **EMEA/H/C/005304/II/0001** AstraZeneca AB, Rapporteur: Thalia Marie Estrup Blicher, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy information based on additional results from study D5290C00004 (MELODY); this is a Phase	Request for supplementary information adopted with a specific timetable.

III Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of MEDI8897, for the Prevention of Medically Attended Lower Respiratory Tract Infection Due to Respiratory Syncytial Virus in Healthy Late Preterm and Term Infants." Request for Supplementary Information adopted on 26.01.2023.	
Calquence - acalabrutinib - EMEA/H/C/005299/II/0013 AstraZeneca AB, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final results from study ACE-CL-309 (A Phase 3 randomized open-label active-control study investigating Calquence for the Treatment of Subjects With Relapsed or Refractory Chronic Lymphocytic Leukaemia) listed as a category 3 study in the RMP." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 15.09.2022.	Positive Opinion adopted by consensus on 12.01.2023.
Dupixent - dupilumab - EMEA/H/C/004390/II/0068 Sanofi Winthrop Industrie, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.8 and 5.1 of the SmPC to include long-term safety and efficacy information in children based on final results from study LTS14424 - EXCURSION. This is an interventional one-year study, to evaluate the long-term safety and tolerability of dupilumab in children 6 to 11 years of age with asthma, who participated in a previous dupilumab asthma clinical study EFC14153." Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
Eliquis - apixaban - EMEA/H/C/002148/II/0088 Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the SmPC in order to update efficacy and safety information in the paediatric population based on results of the paediatric studies performed in compliance with the paediatric investigation plan (PIP), including studies CV185155 and CV185362. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 26.01.2023.	
Enbrel - etanercept - EMEA/H/C/000262/II/0249 Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.6 of the SmPC in order to update information on breast feeding exposure based on the cumulative review of etanercept specific pharmacology, safety database and published medical literature. The Package Leaflet is updated accordingly. In addition, the MAH is taking this opportunity to correct minor administrative and typographical changes to the SmPC, Labelling and Package Leaflet. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Evoltra - clofarabine - EMEA/H/C/000613/II/0077 Genzyme Europe BV, Rapporteur: Alexandre Moreau, "Update of the Package Leaflet in order to update information regarding breast-feeding based on a comprehensive safety review. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 12.01.2023, 08.09.2022.	Request for supplementary information adopted with a specific timetable.
Evrysdi - risdiplam - EMEA/H/C/005145/II/0011, Orphan Roche Registration GmbH, Rapporteur: Bruno Sepodes, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to delete an existing warning on "Use with SMA gene therapy" and to update the safety profile and efficacy data in patients previously treated with other SMA-modifying therapies based on the 24-month primary analysis data from study BP39054 (JEWELFISH); this is a multicentre, open-label study to investigate the safety, tolerability, and pharmacokinetics/pharmacodynamics of risdiplam in adult and paediatric patients with SMA. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 26.01.2023.	
Imfinzi - durvalumab - EMEA/H/C/004771/II/0054 AstraZeneca AB, Rapporteur: Aaron Sosa Mejia, "Submission of final report from non-clinical study ONC4736-PB-0401 (Profiling of Biomarkers Relevant to Immunotherapies in Paediatric Solid Tumours)." Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
INREBIC - fedratinib - EMEA/H/C/005026/II/0010/G, Orphan Bristol-Myers Squibb Pharma EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sonja Hrabcik, "Update of section 4.4 of the SmPC in order to add new warnings on major adverse cardiac events (MACE), thrombosis and secondary malignancies. The updates pertain to three signals, assessed by the FDA, which were identified with another JAK inhibitor (tofacitinib) indicated in rheumatoid arthritis; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 26.01.2023, 10.06.2022.	Request for supplementary information adopted with a specific timetable.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0128 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 5.1 of the SmPC in order to update information based on the final OS data for the overall population as well as for MMR subgroups from study 309/KEYNOTE-775 in order to fulfil the Recommendation: REC/033. This Recommendation was agreed with the approval of study 309/KEYNOTE-775; this is a multicentre, open-label, randomized, phase 3 trial to compare the efficacy and safety of lenvatinib in combination with pembrolizumab versus treatment of physician's choice in participants with advanced endometrial cancer." Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
Lenvima - lenvatinib - EMEA/H/C/003727/II/0049 Eisai GmbH, Rapporteur: Karin Janssen van Doorn, "Update of section 5.1 of the SmPC in order to update the efficacy information of	Request for supplementary information adopted with a specific timetable.

"Endometrial carcinoma" based on the final OS analysis data for the overall population as well as for MMR subgroups from study E7080-G000-309 / KEYNOTE-775. This is a Multicentre, Open-label, Randomized, Phase III study to compare the efficacy and safety of lenvatinib in combination with pembrolizumab versus treatment of physician's choice in participants with advanced endometrial cancer. In addition, the MAH took the opportunity to implement editorial changes in the SmPC." Request for Supplementary Information adopted on 19.01.2023.	
Lynparza - olaparib - EMEA/H/C/003726/II/0057 AstraZeneca AB, Rapporteur: Alexandre Moreau, "Update of sections 4.8 and 5.1 of the SmPC in order to update the long-term safety data and the final OS analysis from PAOLA-1 study (D0817C00003). This is a Randomized, Double-Blind, Phase III Trial of Olaparib vs. Placebo in Patients with Advanced FIGO Stage IIIB – IV High Grade Serous or Endometrioid Ovarian, Fallopian Tube, or Peritoneal Cancer Treated with Standard First Line Treatment, Combining Platinum-Taxane Chemotherapy and Bevacizumab Concurrent with Chemotherapy and in Maintenance. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Lynparza - olaparib - EMEA/H/C/003726/II/0058 AstraZeneca AB, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the olaparib tablet SmPC based on results from study D0816C00020 (OPINION); this is a Phase IIIb single arm, multicentre study, investigating olaparib as a maintenance treatment in patients with platinum sensitive relapsed ovarian, fallopian tube or primary peritoneal cancer following 2 or more lines of platinum-based chemotherapy and who did not have a known deleterious or suspected deleterious gBRCA mutation. The MAH also took the opportunity to make minor editorial corrections to the product information." Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023. See 9.1
Nexpovio - selinexor -	Positive Opinion adopted by consensus on

EMEA/H/C/005127/II/0011 Stemline Therapeutics B.V., Rapporteur: Blanca Garcia-Ochoa, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information regarding the strong CYP3A4 inhibitor, clarithromycin, based on results from the drug-drug interaction (DDI) pharmacokinetic (PK) portion of study KCP 330-017 (STOMP) following procedure EMEA/H/C/005127/REC/003.1. This is a Phase 1b/2, multi-centre, open-label, clinical study with Dose Escalation (Phase 1) and Expansion (Phase 2) to independently assess the MTD, efficacy, and safety of 10 combination therapies in 11 arms in patients with RRMM (Relapsed/Refractory Multiple Myeloma) and NDMM (Newly Diagnosed Multiple Myeloma)." Opinion adopted on 26.01.2023.	26.01.2023.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0035 AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to remove the information referring to healthy volunteers and to add infusion related adverse reactions in bleeding patients following an internal review of the labels and based on ANNEXA-4 study. The Package Leaflet is updated accordingly. In addition, the MAH would like to take this opportunity to make some corrections in the SmPC." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Onpattro - patisiran - EMEA/H/C/004699/II/0025, Orphan Alnylam Netherlands B.V., Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 of the SmPC based on interim results from study ALN-TTR02-006 listed as a category 3 study in the RMP; this is a multicentre, open-label, extension study to evaluate the long-term safety and efficacy of patisiran in patients with familial amyloidotic polyneuropathy who have completed a prior clinical study with patisiran. In addition, the MAH took the opportunity to update section 3 of the SmPC in order to update the pH ." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 12.01.2023.

on 06.10.2022, 23.06.2022.	
Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0026/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Grouped application comprising four type II variations as follows: - Update of section 4.6 to update information related to the nonclinical data on developmental toxicity without change the recommendation based on cases reported on on-going clinical trials C4671002, C4671005 and C4671006, or reported during post-marketing, and the pre- and post-natal development study report 21GR149. - Update of section 5.1 of the SmPC in order to include final clinical efficacy and safety data based on the pivotal C4671005 study. Section 5.1 of the SmPC is also updated to include the antiviral activity of nirmatrelvir, against the sub-variants B.1.1.529/BA.1, BA.2, BA.2.12.1, BA.4, and BA.5, antiretroviral resistance information based on in vitro assays and viral load rebound and treatment-emergent mutations observed in clinical practice. - Update of section 5.2 of the SmPC in order to update pharmacokinetic data on the effect of food on oral absorption following the submission of the results from studies C4671012, C4671013, C467104, C4671015 and C4671019. The first four studies are DDI studies conducted in healthy volunteers, with dabigatran, midazolam, carbamazepine and itraconazole, respectively. C4671019 was a phase 1, open-label, randomised, single dose, 2-sequence, 2-period crossover study to evaluate the effect of high-fat meal on the relative bioavailability of nirmatrelvir boosted with ritonavir following after single oral dose administration in healthy adult participants. The MAH has taken the opportunity to include editorial changes in sections 4.2, 4.5, 4.8 and 6.1 of the SmPC and the Package Leaflet." Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 10.11.2022.	Positive Opinion adopted by consensus on 26.01.2023.
Piqray - alpelisib - EMEA/H/C/004804/II/0017 Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of section 5.3 of the	Positive Opinion adopted by consensus on 12.01.2023.

SmPC in order to update non-clinical information based on data from two skin toxicology studies conducted in rats: study 1770766 and study 1870156." Opinion adopted on 12.01.2023.	
Reblozyl - luspatercept - EMEA/H/C/004444/II/0011, Orphan Bristol-Myers Squibb Pharma EEIG, Rapporteur: Daniela Philadelphy, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to include new safety information about Extramedullary Hematopoietic Masses in transfusion-dependent beta-thalassemia patients based on the open-label phase of the ACE-536-B-THAL-001 Phase III study, the long-term follow-up study and post marketing data. The Package Leaflet is updated accordingly." Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 15.09.2022.	Positive Opinion adopted by consensus on 26.01.2023.
Retsevmo - selpercatinib - EMEA/H/C/005375/II/0016 Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, "Update of section 4.8 of the SmPC in order to add chylothorax and chylous ascites to the list of adverse drug reactions (ADRs) based on a review of adverse events. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 19.01.2023, 06.10.2022.	Request for supplementary information adopted with a specific timetable.
Ronapreve - casirivimab / imdevimab - EMEA/H/C/005814/II/0009 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning for convulsive syncope to the list of adverse drug reactions (ADRs) with frequency not known, following a signal assessment conducted by MAH. The Package Leaflet is updated accordingly." Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0051, Orphan Janssen-Cilag International N.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update information on breast-feeding based on new literature." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable. See 9.1

on 26.01.2023, 15.12.2022.	
Spectrila - asparaginase - EMEA/H/C/002661/II/0032/G medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Christian Gartner, "Grouped Variation (Type II & Type IB): C.I.4: Update of sections 4.4 and 4.6 of the SmPC in order to include the recommendations from the SWP regarding genotoxic medicinal products and contraception duration period; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.6.b: Deletion of the indication lymphoblastic lymphoma (LBL) in section 5.3 of the SmPC, as Spectrila is not approved for LBL." Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
Spikevax - elasomeran - EMEA/H/C/005791/II/0088 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study DMID 20-0003 listed as a category 3 study in the RMP. This is a Phase I, Open Label, Dose-ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (mRNA-1273) in Healthy Adults." Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
Taltz - ixekizumab - EMEA/H/C/003943/II/0046 Eli Lilly and Co (Ireland) Limited, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to add 'oesophageal candidiasis' to the list of adverse drug reactions (ADRs) with frequency rare based on a safety review of all associated data; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and update instructions for use to clarify information on product stability at room temperature." Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
TEZSPIRE - tezepelumab - EMEA/H/C/005588/II/0004 AstraZeneca AB, Rapporteur: Finbarr Leacy, "Submission of the final report detailing the	Request for supplementary information adopted with a specific timetable.

extended follow-up data from study D5180C00018 (DESTINATION) listed as a category 3 study in the RMP; this is a multicentre, randomised, double-blind, placebo-controlled, parallel group, long term extension study designed to evaluate the safety and efficacy of 210 mg Q4W subcutaneous of tezepelumab in adults and adolescents with severe uncontrolled asthma for up to 2 continuous years of treatment." Request for Supplementary Information adopted on 26.01.2023.	
TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0018/G Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus, "Grouped application comprising two type II variations as follows: - To update section 4.8 of the SmPC based on an integrated summary of immunogenicity. - To update sections 4.5 and 5.2 of the SmPC based on data on the impact of concomitant medications including UGT1A1 inhibitors/inducers on SN-38 pharmacokinetic (PK) based on the PopPK model refinement." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 08.12.2022.	Positive Opinion adopted by consensus on 12.01.2023.
Vargatef - nintedanib - EMEA/H/C/002569/II/0047/G Boehringer Ingelheim International GmbH, Rapporteur: Aaron Sosa Mejia, "Grouped application containing: C.I.4: Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to update information regarding the paediatric population based on results from study 1199-0337; this is a double blind, randomised, placebo-controlled trial to evaluate the dose-exposure and safety of nintedanib on top of standard of care for 24 weeks, followed by open label treatment with nintedanib of variable duration, in children and adolescents (6 to 17 year-old) with clinically significant fibrosing interstitial lung disease. The Package Leaflet is updated accordingly. C.I.4: Update of sections 4.2 and 5.2 of the SmPC in order to improve the recommendation for the administration of nintedanib based on food compatibility data. The Package Leaflet is updated accordingly.	Request for supplementary information adopted with a specific timetable.

In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 26.01.2023.	
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0110 MCM Vaccine B.V., Rapporteur: Christophe Focke, "Update of section 4.8 of the SmPC in order to add 'hypersensitivity' and 'anaphylactic reaction' to the list of adverse drug reactions (ADRs) with frequency not known based on the safety assessment of post-marketing reports of hypersensitivity including anaphylactic reactions; the Package Leaflet is updated accordingly." Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 15.12.2022.	Positive Opinion adopted by consensus on 26.01.2023.
Vaxneuvance - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477/II/0011 Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, "To update sections 4.2 and 5.1 of the SmPC in order to update the information for immune response after subcutaneous administration based on final results from study V114-P033 (EudraCT: 2019-003644-68), in accordance with Article 46 of the paediatric regulation. V114-P033 is a phase 3 Active-Comparator controlled study to evaluate the Safety, Tolerability, and Immunogenicity of V114 in Healthy Japanese Infants. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable. See 9.1
Verzenios - abemaciclib - EMEA/H/C/004302/II/0024 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to include overall survival data based on final results from study MONARCH 2; this is a randomized, double-blind, placebo-controlled, phase 3 study of fulvestrant with or without abemaciclib, a CDK4/6 Inhibitor, for women	Positive Opinion adopted by consensus on 26.01.2023.

with hormone receptor-positive, HER2-negative locally advanced or metastatic breast cancer." Opinion adopted on 26.01.2023.	
VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0026 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.8 and 5.1 of the SmPC in order to add 'headache' to the list of adverse drug reactions (ADRs) with frequency very common and to update information based on final results from study 071301 and other available data; study 071301 is a prospective, phase 3, open-label, international multicentre study on efficacy and safety of prophylaxis with rVWF in severe von Willebrand disease. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce minor editorial changes to the PI and bring it in line with the latest QRD template." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 20.10.2022.	Positive Opinion adopted by consensus on 12.01.2023.
VPRIV - velaglucerase alfa - EMEA/H/C/001249/II/0054 Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Martina Weise, "Submission of the final report from study SHP-GCB-402: a multicentre, open-label, single-arm, phase 4 study designed to prospectively evaluate the effects of VPRIV on bone-related pathology in treatment-naïve subjects with type 1 Gaucher disease." Request for Supplementary Information adopted on 12.01.2023, 28.04.2022.	Request for supplementary information adopted with a specific timetable.
XALKORI - crizotinib - EMEA/H/C/002489/II/0078 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Submission of the final report from study A8081001 (A Phase 1 Safety, Pharmacokinetic and Pharmacodynamic Study Of PF-02341066, A MET/HGFR Selective Tyrosine Kinase Inhibitor, Administered Orally to Patients with Advanced Cancer), to fulfil recommendation 8 of the Xalkori MAA to further investigate the role of c-Met status in ALK-negative patients."	Positive Opinion adopted by consensus on 26.01.2023.

Opinion adopted on 26.01.2023.	
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0096 Bayer AG, Rapporteur: Kristina Dunder, "Submission of the final report from study 15786 (COMPASS LTOLE). This is a phase 3, multicentre, randomized, double-blind, double-dummy, active comparator, event-driven study, in which subjects were randomized 1:1:1 to rivaroxaban 2.5 mg bid/ASA 100 mg od, or rivaroxaban 5 mg bid, or ASA 100 mg od." Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 13.10.2022.	Positive Opinion adopted by consensus on 26.01.2023.
Zercepac - trastuzumab - EMEA/H/C/005209/II/0020 Accord Healthcare S.L.U., Rapporteur: Sol Ruiz, "Submission of the final report from study HLX02-BC01 in order to fulfil REC/006. This is a double-blind, randomised, parallel-controlled, multicentre, international, phase 3 study to compare the efficacy, safety, and immunogenicity of HLX02 versus EU-sourced Herceptin in combination with docetaxel." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 12.01.2023.
WS2358 **Elebrato Ellipta- EMEA/H/C/004781/WS2358/0028** **Trelegy Ellipta- EMEA/H/C/004363/WS2358/0025** GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Finbarr Leacy, "Update of section 4.8 of the SmPC in order to add 'urinary retention' and 'dysuria' to the list of adverse drug reactions (ADRs) with frequency rare; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and bring it in line with the latest QRD template." Request for Supplementary Information adopted on 12.01.2023, 10.11.2022.	Request for supplementary information adopted with a specific timetable.
WS2377 **Jentadueto- EMEA/H/C/002279/WS2377/0067** **Synjardy- EMEA/H/C/003770/WS2377/0067**	Request for supplementary information adopted with a specific timetable.

Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on Vitamin B12 decrease or deficiency and to update the list of adverse drug reactions (ADRs) in accordance with the recent update of the PI for Glucophage, which is the reference label for the compound metformin, and following the request by MHRA on 20 June 2022 for all products containing metformin; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 12.01.2023.	

B.5.3. CHMP-PRAC assessed procedures

Beovu - brolucizumab - EMEA/H/C/004913/II/0021 Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendation in including an additional dose regimen (q16w) for DME patients during the maintenance phase, update the frequency of adverse drug reactions, update pharmacokinetic, pharmacodynamic, efficacy and safety information, following the assessment of procedure II/10, based on final results from studies CRTH258B2301 (KESTREL) and CRTH258B2302 (KITE). The Package Leaflet is updated accordingly. The RMP version 10 has also been submitted." Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Cablivi - caplacizumab - EMEA/H/C/004426/II/0040, Orphan Ablynx NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to update information on long-term efficacy and safety based on final results from study ALX0681-C302/LTS16371 - Prospective Follow-up Study for Patients who Completed Study ALX0681-C301 (HERCULES) to Evaluate Long-term Safety and Efficacy of Caplacizumab (Post-	Positive Opinion adopted by consensus on 12.01.2023.

HERCULES), listed as a category 3 study in the RMP. The Post-HERCULES study was a Phase III, 36-month follow-up study from HERCULES (parent study) to evaluate the long-term outcomes as well as the safety and efficacy of repeat use of caplacizumab in patients who experienced a recurrence of aTTP. The RMP version 3.0 has also been submitted." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 01.12.2022.	
Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0099 Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of adverse drug reactions (ADRs), add Pseudomeningocele to the list of ADRs with frequency uncommon and to update efficacy and safety information on the paediatric population, following P46/0030 based on the final results from the paediatric clinical study BIOS-13-006. This is a Prospective Randomized Controlled Study Evaluating the Safety and Efficacy of EVICEL used for Suture- Line Sealing in Dura-Mater Closure during Paediatric Neurosurgical Cranial Procedures. The Package Leaflet is updated accordingly. Editorial changes are proposed to sections of the product information. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.3. The RMP version 15 has also been submitted." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Fintepla - fenfluramine - EMEA/H/C/003933/II/0015, Orphan Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, "To update sections 4.2 and 5.2 of the SmPC to update the safety information based on final results from study ZX008-1903 listed as a category 3 study in the RMP; this is a Phase 1, Open-Label, Single-Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of ZX008 (Fenfluramine Hydrochloride) in Subjects with Varying Degrees of Hepatic Impairment.	Request for supplementary information adopted with a specific timetable.

The primary objective of this study was to compare the PK of a single dose of ZX008 (fenfluramine HCl) in subjects with varying degrees of hepatic impairment with that of healthy matched control subjects. The updated RMP version 2.7 has also been submitted." Request for Supplementary Information adopted on 12.01.2023, 29.09.2022.	
GIVLAARI - givosiran - EMEA/H/C/004775/II/0011/G, Orphan Alnylam Netherlands B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber, "Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-007 listed as a category 3 study in the RMP; This is a 104-week Subcutaneous Injection Carcinogenicity Study in Sprague Dawley Rats. Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-004; This is a 26-week Subcutaneous Injection Carcinogenicity Study in TgRasH2 Mice. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 12.01.2023, 29.09.2022.	Request for supplementary information adopted with a specific timetable.
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0059, Orphan CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update information and amend the frequencies of adverse drug reactions (ADRs) based on the final results from study CSL654_3003 listed as a category 3 study in the RMP; this is an open-label, multicentre, uncontrolled study to evaluate the safety, pharmacokinetics and clinical response of rIX-FP with regard to the prevention and treatment of bleeding in previously untreated patients (PUPs) with Haemophilia B. The Package Leaflet is updated accordingly. The RMP version 4.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and update the list of local representatives in the Package Leaflet."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 12.01.2023, 27.10.2022, 10.06.2022.	
Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0036 Almirall S.A, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Adam Przybylkowski Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 27.10.2022.	Positive Opinion adopted by consensus on 26.01.2023.
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0056 Orexigen Therapeutics Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, "Submission of updated study design and protocol synopsis for CVOT-2 study, a category 1 study listed in Annex II.D (ANX/001.7) undertaken to assess the effect of naltrexone extended release (ER) / bupropion ER on the occurrence of major adverse cardiovascular events (MACE), as requested in the CHMP AR for ANX/001.6. The Annex II and the RMP version 13 are updated accordingly." Request for Supplementary Information adopted on 26.01.2023, 15.09.2022, 24.03.2022.	Request for supplementary information adopted with a specific timetable. See 9.1
NINLARO - ixazomib - EMEA/H/C/003844/II/0041, Orphan Takeda Pharma A/S, Rapporteur: Armando Genazzani, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study NSMM-5001 (INSIGHT) listed as a Specific Obligation in the Annex II of the Product Information. This is a global, prospective, non-interventional, observational study of presentation, treatment patterns, and outcomes in multiple myeloma patients. The Annex II and the RMP (submitted version 9.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. The requested variation proposed amendments to the Annex II and to the Risk Management Plan (RMP)." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 29.09.2022.	Positive Opinion adopted by consensus on 12.01.2023.
NUBEQA - darolutamide -	Positive Opinion adopted by consensus on

EMEA/H/C/004790/II/0012 Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Jan Neuhauser, "Update of section 5.3 of the SmPC based on the final report of carcinogenicity study T104877-7 listed as a category 3 study in the RMP. This is a non-clinical study to assess the carcinogenic potential in mice. The study evaluates the effects of daily oral administration of darolutamide for a period of 6 months in tg-rasH2 transgenic mouse model. The updated RMP version 3.2 is approved." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 01.12.2022, 01.09.2022.	12.01.2023.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0033 AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Update of section 5.1 of the SmPC based on interim results from study PK/PD study listed as a specific obligation in the Annex II in order to fulfil SOB 1 and SOB 3; this is a PK and PK/PD Analysis of Intravenously Administered Andexanet after dosing to steady state with a factor Xa inhibitor, rivaroxaban or Apixaban, in healthy subjects and patients who have acute major bleeding. In addition, the MAH took the opportunity implement editorial changes in Annex II of the SmPC. The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 26.01.2023, 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Polivy - polatuzumab vedotin - EMEA/H/C/004870/II/0018, Orphan Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study GO29365 listed as a category 3 study in the RMP in order to address MEA/002. This is a phase Ib/II, multicentre, open-label study evaluating the safety, tolerability, and anti-tumour activity of polatuzumab vedotin in combination with rituximab or obinutuzumab plus bendamustine in patients with R/R follicular lymphoma or R/R diffuse large B-cell lymphoma. The RMP version 3.0 has also been submitted." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 12.01.2023.

on 29.09.2022.	
QINLOCK - ripretinib - EMEA/H/C/005614/II/0004, Orphan Deciphera Pharmaceuticals (Netherlands) B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Željana Margan Koletić, "Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in patients with hepatic impairment and update the description of pharmacokinetics based on final results from study DCC-2618-01-004; a Phase 1 study of the Pharmacokinetics, Safety, and Tolerability of Ripretinib in Subjects With Hepatic Impairment Compared to Healthy Control Subjects. The Package Leaflet is updated accordingly. The RMP version 2.2 has also been submitted." Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 15.09.2022.	Positive Opinion adopted by consensus on 26.01.2023.
Rozlytrek - entrectinib - EMEA/H/C/004936/II/0014 Roche Registration GmbH, Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.2 of the SmPC in order to update the pharmacokinetic information based on final results from study GP411174 listed as an additional pharmacovigilance activity in the RMP; this is a Phase I, non-randomized, single-dose, open-label study to investigate the effect of impaired hepatic function on the pharmacokinetics of entrectinib in volunteers with different levels of hepatic function. The RMP version 4.1 has also been agreed. In addition, the MAH took the opportunity to update in Annex II section C and to update the list of local representatives in the Package Leaflet." Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.
Simponi - golimumab - EMEA/H/C/000992/II/0109 Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the Package Leaflet in order to update the Instructions for Use (IFU) for the pre-filled pen." Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.

Stelara - ustekinumab - EMEA/H/C/000958/II/0096 Janssen-Cilag International N.V., Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, "Update of section 5.1 of the SmPC in order to update information with the 4-year clinical data in patients with ulcerative colitis based on the final report from study CNTO1275UCO3001 listed as a category 3 study in the RMP; this is a phase 3, randomized, double blind, placebo-controlled, parallel-group, multicentre study to evaluate the safety and efficacy of ustekinumab induction and maintenance therapy in subjects with moderately to severely active ulcerative colitis. The RMP version 23.1 has also been submitted. In addition, the MAH took the opportunity to introduce a correction to the PI." Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0075 Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add 'pericardial disorders' to the list of adverse drug reactions (ADRs) with frequency common in monotherapy and uncommon in combination therapy based on the final results from Drug Safety Report (DSR 1115896) including review of available clinical trial data, post-marketing data and literature. In addition, the MAH took the opportunity to update Annex II section D of the SmPC to refer to immune-mediated adverse reactions and to implement editorial changes in the SmPC. The Package Leaflet was updated accordingly. The RMP version 23.1 has also been agreed." Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.
Translarna - ataluren - EMEA/H/C/002720/II/0069, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, "Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information following results from study PTC124-GD-041-DMD, listed as a specific obligation in the Annex II; This is a Phase 3 multicentre, randomised, double-blind,	Request for supplementary information adopted with a specific timetable. See 9.1

18-month, placebo-controlled study, followed by a 18-month open label extension to confirm the efficacy and safety of ataluren in the treatment of ambulant patients with mnDMD aged 5 years or older. Annex II, and Annex IIB are updated to delete the SOB and to reflect the switch from conditional to full marketing authorisation. The Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted. Minor corrections were done to align the PI with the latest QRD templates." Request for Supplementary Information adopted on 26.01.2023.	
Vaxneuvance - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477/II/0013/G Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Grouped application comprising two type II variations as follows: - To update sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to add safety data on recipients of haematopoietic stem cell transplant (HSCT) based on final results from study V114-022, listed as a category 3 study in the RMP; This is a Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of Vaxneuvance in Recipients of Allogeneic Hematopoietic Stem Cell Transplant. - To update sections 4.2 and 5.1 of the SmPC in order to update the information regarding a 3-dose regimen based on final results from study V114-026; a Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of a 3-dose Regimen of Vaxneuvance in Healthy Infants. The Package Leaflet is updated accordingly. The RMP version 2.1 has also been submitted." Request for Supplementary Information adopted on 26.01.2023.	Request for supplementary information adopted with a specific timetable.
Zeposia - ozanimod - EMEA/H/C/004835/II/0016 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon, "Update of sections 4.2 and 5.2 of the SmPC in order to add a dose adjustment after completion of the dose escalation regimen	Request for supplementary information adopted with a specific timetable.

in patients with mild or moderate chronic hepatic impairment (Child-Pugh class A or B) based on the final results from study RPC-1063-CP-004; this is a Phase I, multicentre, open-label study to evaluate the effect of mild or moderate hepatic impairment on the multiple-dose pharmacokinetics of ozanimod. The Package Leaflet is updated accordingly. The updated RMP version 5.0 has also been submitted." Request for Supplementary Information adopted on 26.01.2023.	
WS2307 **Rixathon-** **EMEA/H/C/003903/WS2307/0062** **Riximyo-** **EMEA/H/C/004729/WS2307/0063** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Anette Kirstine Stark, "Update of section 4.1 of the SmPC in order to include the rapid infusion regimen (90 minutes) for second and subsequent infusions in the label for patients with non-Hodgkin's lymphoma (NHL) or chronic lymphocytic leukaemia (CLL) based on non-interventional PASS CGP2013ES01R and scientific literature. The RMP version 7.0 has also been submitted." Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 15.09.2022.	Positive Opinion adopted by consensus on 26.01.2023.

B.5.4. PRAC assessed procedures

PRAC Led **Alecensa - alectinib -** **EMEA/H/C/004164/II/0044** Roche Registration GmbH, PRAC Rapporteur: Jana Lukacisinova, PRAC-CHMP liaison: Ondřej Slanař, "Submission of an updated RMP version 3.3 in order to remove the important identified risks of Interstitial Lung Disease (ILD)/Pneumonitis, Hepatotoxicity, Photosensitivity, Bradycardia, Severe myalgia and Creatine Phosphokinase (CPK) elevations as well as the important potential risk of Embryo-foetal toxicity as safety concerns. Furthermore, template updates in line with the GVP Product or Population-Specific Considerations III: Pregnant and breastfeeding women are made."	Positive Opinion adopted by consensus on 12.01.2023.

Opinion adopted on 12.01.2023.	
PRAC Led **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0152** BioNTech Manufacturing GmbH, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to add "Dizziness" to the list of adverse drug reactions (ADRs) with frequency 'Uncommon', based on a cumulative review. The Package Leaflet is updated accordingly." Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
PRAC Led **Cotellic - cobimetinib - EMEA/H/C/003960/II/0027** Roche Registration GmbH, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of sections 4.4 and 5.1 of the SmPC in order to update information based on final results from study ML39302 listed as a category 3 study in the RMP in order to fulfil MEA/003.5; this is a non-interventional PASS study to investigate the effectiveness, safety and utilization of cobimetinib and vemurafenib in patients with and without brain metastasis with BRAF V600 mutant melanoma under real world conditions. The RMP version 5.0 has also been submitted." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 12.01.2023.
PRAC Led **Fintepla - fenfluramine - EMEA/H/C/003933/II/0017, Orphan** Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP version 2.10 in order to implement a targeted follow-up questionnaire (FUQ) to further improve the collection of follow-up information on cases of vascular heart disease (VHD) and pulmonary arterial hypertension (PAH) suggested by PRAC following the assessment of procedure EMEA/H/C/PSUSA/00010907/202112." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.

PRAC Led **IMVANEX - smallpox vaccine (live modified vaccinia virus ankara) - EMEA/H/C/002596/II/0081** Bavarian Nordic A/S, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 9.1 in order to update the safety specifications in line with extension of the indication to "active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in adults", update the missing information from the list of safety concerns, differentiate routine pharmacovigilance activities and additional pharmacovigilance activities, addition of non-BN sponsored clinical study SEMVAc to additional pharmacovigilance activities and deletion of paediatric study POX-MVA-035 upon request by PRAC following the assessment of procedure II/76." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **NutropinAq - somatropin - EMEA/H/C/000315/II/0077** Ipsen Pharma, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of an updated RMP version 4.0 in order to remove some of the safety concerns in compliance with GVP Module V Revision 2. In addition, the MAH took the opportunity to add data from final clinical study report of International Cooperative Growth Study (iNCGS) registry (non-interventional study) and exposure and safety information." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Olumiant - baricitinib - EMEA/H/C/004085/II/0031** Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "Submission of the final study report from study I4V-MC-B023, a non-interventional PASS which provided a comparative assessment of VTE and other risks among patients with rheumatoid arthritis with	Positive Opinion adopted by consensus on 26.01.2023.

baricitinib versus TNF inhibitors listed as category 3 in the RMP. An RMP (version 18.2) has also been updated." Opinion adopted on 26.01.2023. Request for Supplementary Information adopted on 22.04.2022, 13.01.2022.	
PRAC Led **Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0032** Pfizer Europe MA EEIG, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Update of section 4.8 of the SmPC in order to add 'hypertension' to the list of adverse drug reactions (ADRs) with frequency 'uncommon', following procedure EMEA/H/C/005973/LEG/006, based on review of aggregate post-marketing data. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Sialanar - glycopyrronium - EMEA/H/C/003883/II/0026** Proveca Pharma Limited, PRAC Rapporteur: Zane Neikena, PRAC-CHMP liaison: Elita Poplavska, "Submission of an updated RMP version 3.1 in order to remove a Drug Utilisation Study (DUS)." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Spikevax - elasomeran - EMEA/H/C/005791/II/0085/G** Moderna Biotech Spain, S.L., PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Grouped application comprising two type II variations as follows: C.I.11.b - To add Spikevax bivalent Original/ Omicron BA.4-5 vaccine (mRNA-1273.222), to update studies mRNA-1273-P904, mRNA-1273-P905 and mRNA-1273-P910 in the Pharmacovigilance Plan to include exposure to Spikevax bivalent vaccines, to update the INN to elasomeran/davesomeran, and to reclassify studies mRNA-1273-P205 from category 2 to category 3 studies in the Pharmacovigilance Plan. C.I.13 - To submit the final CSR from study	Request for supplementary information adopted with a specific timetable.

mRNA-1273-P201, a Phase 2a, Randomized, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults ≥= 18 Years listed as a category 3 study including addition of clinical trial exposure data for part C of the study mRNA-1273-P201. RMP version 6.0 will be updated accordingly." Request for Supplementary Information adopted on 12.01.2023.	
PRAC Led **Stivarga - regorafenib - EMEA/H/C/002573/II/0039** Bayer AG, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to remove the disease specific precaution for hepatocellular carcinoma based on final results from study REFINE (study number 19244) listed as a category 3 study in the RMP; this is an international, prospective, open-label, multi-centre, observational study to describe the safety and effectiveness of treatment with regorafenib in real-world settings. The RMP version 6.1 has also been submitted." Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
PRAC Led **Stocrin - efavirenz - EMEA/H/C/000250/II/0130** Merck Sharp & Dohme B.V., Duplicate, Duplicate of Sustiva, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of an updated RMP version 9.0 in accordance with the new template and thereby to remove safety concerns." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **SYLVANT - siltuximab - EMEA/H/C/003708/II/0038, Orphan** EUSA Pharma (Netherlands) B.V, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the report from study ACCELERATE (Advancing Castleman Care with an Electronic Longitudinal Registry, E-Repository, And Treatment/Effectiveness Research): An International Registry for Patients with Castleman Disease -	Positive Opinion adopted by consensus on 12.01.2023.

NCT02817997 listed as an obligation in the Annex II of the Product Information. This is a study report to cover the data collected for 100 patients over a 5-year period in the ACCELERATE Registry study to collect information or patients with Castleman's Disease who are candidates to receive Sylvant or are currently receiving treatment with Sylvant. The obligation has now been fulfilled, the Annex II is updated accordingly." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 27.10.2022.	
PRAC Led **Tarceva - erlotinib - EMEA/H/C/000618/II/0071** Roche Registration GmbH, PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Aaron Sosa Mejia, "Update of section 4.8 of the SmPC in order to provide a single table listing all ADRs following PSUSA/00001255/202111. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS2270 Vfend-EMEA/H/C/000387/WS2270/0147** Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "To update the Annex II and RMP to version 6.0 to include the results from the final clinical study report (CSR) following the completion of a non-interventional (NI) post-authorisation safety study (PASS), A1501103 "An Active Safety Surveillance Program to Monitor Selected Events in Patients with Long-term Voriconazole Use" - MEA091. In addition, the MAH is taking this opportunity to introduce editorial changes." Request for Supplementary Information adopted on 12.01.2023, 01.09.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS2320 Stribild-EMEA/H/C/002574/WS2320/0120 Truvada-**	Positive Opinion adopted by consensus on 12.01.2023.

EMEA/H/C/000594/WS2320/0177 Gilead Sciences Ireland UC, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "To update Annex II and the RMP for Truvada and Stribild to version 18.1 and 14.1 to remove of the paediatric additional Risk Minimisation Measures (aRMMs) for the HIV indication. In addition, the MAH took the opportunity to introduce changes to the PI." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 29.09.2022.	
PRAC Led **WS2356** **Epclusa-EMEA/H/C/004210/WS2356/0068** **Harvoni-EMEA/H/C/003850/WS2356/0107** **Sovaldi-EMEA/H/C/002798/WS2356/0081** **Vosevi-EMEA/H/C/004350/WS2356/0057** Gilead Sciences Ireland UC, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "To provide an updated RMP, following finalisation of procedure EMEA/H/C/WS2222 providing the final CSR for the non-imposed joint PASS study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (study B20-146). In particular, the list of safety concerns has been updated to remove the important potential risks: "Recurrence of hepatocellular carcinoma (HCC)" and "Emergence of HCC", and to remove "safety in patients with previous HCC" as an area of missing information. In addition, the completed PASS studies: DAA PASS and De Novo DAA PASS have been removed from the pharmacovigilance plan." Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
PRAC Led **WS2369** **Filgrastim Hexal-EMEA/H/C/000918/WS2369/0066** **Zarzio-EMEA/H/C/000917/WS2369/0067** Sandoz GmbH, Lead PRAC Rapporteur: Menno van der Elst, ""C.I.11.z - To amend the RMP to reduce the list of safety concerns and remove risks which are well characterised and already	Positive Opinion adopted by consensus on 12.01.2023.

included in the product information, following PRAC Assessment Report of PSUR P14 (EMEA/H/C/PSUSA/00001391/202109) dated 05-May-2022. Additionally, the due date of the final study report EP06-501 (MEA007) has been updated. Furthermore, the MAH took the opportunity to introduce the following editorial changes: - Removal of pharmaceutical forms and strengths no longer registered in Japan; - Editorial changes in Part V "Risk minimisation measures"." Opinion adopted on 12.01.2023. Request for Supplementary Information adopted on 01.12.2022.	
PRAC Led **WS2378** **Exelon-EMEA/H/C/000169/WS2378/0140** **Prometax-EMEA/H/C/000255/WS2378/0141** Novartis Europharm Limited, Lead PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "C.I.11.z - To amend the RMP to: - remove the standalone multiple patch use annual report as an additional pharmacovigilance activity from the Exelon/Prometax RMP, which was endorsed by PRAC (EMA/CHMP/PRAC/342229/2021) on 22-Jul-2021. - include the initial risks reviewed at the time of initial marketing authorisation that were agreed to within RMP Version 1.1 (final: 16-Jul-2007); and the rationale for the removal of some safety concerns from the currently approved RMP Version 10.0, following the PRAC Assessment Report from the currently approved RMP (version 10.0) (EMEA/H/C/XXX/WS/1773). Furthermore, the MAH took the opportunity to introduce editorial changes in the following sections of the RMP: - epidemiology literature, where relevant (Module SI, Epidemiology of the indications and target populations). - worldwide reporting rate of cases of current safety concerns for rivastigmine, as of the latest data lock point of 31-Jan-2022 (Module SV.1, Post-authorisation exposure). - editorial update of preventability of current safety concerns for rivastigmine to reflect the	Positive Opinion adopted by consensus on 12.01.2023.

existing educational material (Module SVII.3, Details of important identified risks, important potential risks, and missing information). The requested work-sharing procedure proposed amendments to the None and to the Risk Management Plan (RMP).” Opinion adopted on 12.01.2023.	

B.5.5. CHMP-CAT assessed procedures

Upstaza - eladocagene exuparvovec - EMEA/H/C/005352/II/0005/G, Orphan, ATMP PTC Therapeutics International Limited, Rapporteur: Maura O'Donovan, CHMP Coordinator: Finbarr Leacy Request for Supplementary Information adopted on 20.01.2023.	Request for supplementary information adopted with a specific timetable.
Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0057, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, Request for Supplementary Information adopted on 20.01.2023.	Request for supplementary information adopted with a specific timetable.

B.5.6. CHMP-PRAC-CAT assessed procedures

Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0033/G, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce additional guidance on liver function laboratory tests and monitoring before and after infusion and update information based on new safety information on the topic of acute liver failure (ALF) following two reports of fatal ALF. Update of sections 4.2 and 4.4 of the SmPC in order to provide additional guidance relevant to patient’s overall health status prior to dosing and to strengthen the existing description and guidance on systemic immune response. Update of section 4.4 of the SmPC in order to indicate prompt attention to thrombotic microangiopathy (TMA) and to reflect the risk of	Positive Opinion adopted by consensus on 26.01.2023.

life-threatening or fatal outcomes. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to update the Annex II." Opinion adopted on 26.01.2023, 20.01.2023. Request for Supplementary Information adopted on 04.11.2022.	

B.5.7. PRAC assessed ATMP procedures

PRAC Led **Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0059, ATMP** Amgen Europe B.V., PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 10 in order to update and reclassify identified risk of 'Disseminated herpetic infection' based on the cumulative assessment of literature review and MAH Global Safety Database and to remove studies 20180062 and 20180099 from Planned and Ongoing Studies from the list of Pharmacovigilance Plan studies in the Annex II." Request for Supplementary Information adopted on 20.01.2023.	Request for supplementary information adopted with a specific timetable.

B.5.8. Unclassified procedures and worksharing procedures of type I variations

WS2276 **Herceptin-EMEA/H/C/000278/WS2276/0186** **Phesgo-EMEA/H/C/005386/WS2276/0015** Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
WS2361 **HBVAXPRO-EMEA/H/C/000373/WS2361/0080** **Vaxelis-EMEA/H/C/003982/WS2361/0112** MCM Vaccine B.V., Lead Rapporteur: Christophe Focke Opinion adopted on 19.01.2023.	Positive Opinion adopted by consensus on 19.01.2023.
WS2363/G **Copalia-EMEA/H/C/000774/WS2363/0127/G** **Dafiro-EMEA/H/C/000776/WS2363/0131/G**	Request for supplementary information adopted with a specific timetable.

Exforge- **EMEA/H/C/000716/WS2363/0126/G** Novartis Europharm Limited, Lead Rapporteur: Thalia Marie Estrup Blicher Request for Supplementary Information adopted on 26.01.2023, 01.12.2022.	
WS2366 **Flebogamma DIF-** **EMEA/H/C/000781/WS2366/0074** Instituto Grifols, S.A., Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
WS2381 **Hexacima-** **EMEA/H/C/002702/WS2381/0142** **Hexyon-** **EMEA/H/C/002796/WS2381/0146** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.
WS2382 **Ebymect-** **EMEA/H/C/004162/WS2382/0060** **Xigduo-EMEA/H/C/002672/WS2382/0070** AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "To update sections 4.2, 4.4 and 5.1 of Xigduo and Ebymect SmPCs to harmonise the applicable dapagliflozin-specific information in the Xigduo and Ebymect QRDs with the Forxiga (dapagliflozin) product information, which has undergone several updates via procedure DAPA-HF (EMEA/H/C/002322/WS1737) and DAPA-CKD (EMEA/H/C/002322/WS1941). Wording approved for Forxiga in these procedures are proposed for the combination products. In addition, the revised QRDs also include proposals for other administrative changes. The corresponding sections 2 and 4 of the PIL have also been updated." Opinion adopted on 12.01.2023.	Positive Opinion adopted by consensus on 12.01.2023.
WS2392/G **Efficib-** **EMEA/H/C/000896/WS2392/0109/G** **Janumet-** **EMEA/H/C/000861/WS2392/0108/G** **Ristfor-** **EMEA/H/C/001235/WS2392/0097/G** **Velmetia-** **EMEA/H/C/000862/WS2392/0114/G**	Request for supplementary information adopted with a specific timetable.

Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 12.01.2023.	
WS2397/G **Incresync-** **EMEA/H/C/002178/WS2397/0045/G** **Vipdomet-** **EMEA/H/C/002654/WS2397/0042/G** **Vipidia-** **EMEA/H/C/002182/WS2397/0034/G** Takeda Pharma A/S, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.
WS2399/G **Mirapexin-** **EMEA/H/C/000134/WS2399/0104/G** **Sifrol-** **EMEA/H/C/000133/WS2399/0095/G** Boehringer Ingelheim International GmbH, Lead Rapporteur: Thalia Marie Estrup Blicher Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
WS2400 **Lixiana-EMEA/H/C/002629/WS2400/0041** **Roteas-EMEA/H/C/004339/WS2400/0028** Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro, Opinion adopted on 19.01.2023.	Positive Opinion adopted by consensus on 19.01.2023.
WS2403 **Kaftrio-EMEA/H/C/005269/WS2403/0032** **Symkevi-** **EMEA/H/C/004682/WS2403/0036** Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 26.01.2023.	Positive Opinion adopted by consensus on 26.01.2023.

B.5.9. Information on withdrawn type II variation / WS procedure

ARIKAYCE liposomal - amikacin - EMEA/H/C/005264/II/0010, Orphan Insmed Netherlands B.V., Rapporteur: Jayne Crowe, PRAC Rapporteur: Jean-Michel Dogné, "Submission of an updated RMP version 1.1 in order to revise the existing specific adverse drug reaction follow-up forms to increase and improve the collection of information related to all four known safety concerns, and to set	The MAH withdrew the procedure on 19.01.2023.

conditions to assess the impact on patient's knowledge and behaviour of the additional risk minimisation measure (patient alert card) implemented for one of the safety concerns (identified risk of allergic alveolitis), as well as to update clinical trial and post-marketing exposure information." Withdrawal request submitted on 19.01.2023.	
VidPrevtyn Beta - SARS-CoV-2, B.1.351 variant, prefusion Spike delta TM protein, recombinant - EMEA/H/C/005754/II/0001/G Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 15.12.2022. Withdrawal request submitted on 19.01.2023.	The MAH withdrew the procedure on 19.01.2023.

B.5.10. Information on type II variation / WS procedure with revised timetable

NUVAXOVID - NVX-CoV2373 - EMEA/H/C/005808/II/0030 Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege, "Submission of 6-month efficacy and safety interim data from the ongoing randomized, observer-blinded, placebo-controlled clinical studies 2019nCoV-501, 2019nCoV-301 and 2019nCoV-302." Request for Supplementary Information adopted on 15.12.2022.	Request by the applicant for an extension to the clock stop to respond to the RSI adopted in December 2022. The CHMP agreed to the request by the applicant.
WS2368 **Invokana- EMEA/H/C/002649/WS2368/0061** **Vokanamet- EMEA/H/C/002656/WS2368/0066** Janssen-Cilag International N.V., Lead Rapporteur: Martina Weise, "To update section 4.4 of the SmPC in order amend an existing warning on the diabetic ketoacidosis, to indicate that glucosuria may persist longer than expected and that DKA may be prolonged after discontinuation of canagliflozin in some patients based on a cumulative review of literature, MAH global safety database, preclinical and clinical pharmacology data, and clinical study data including cases reports." Request for Supplementary Information adopted on 08.12.2022.	Request by the applicant for an extension to the clock stop to respond to the RSI adopted in December 2022. The CHMP agreed to the request by the applicant.
LIVOGIVA - teriparatide -	The CHMP did not agree to the request by the

EMEA/H/C/005087/II/0010 Theramex Ireland Limited, Rapporteur: Daniela Philadelphy Request for Supplementary Information adopted on 15.09.2022, 23.06.2022.	MAH for an extension to the clock stop to respond to the RSI adopted in September 2022. See 9.1

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

B.6.1. Start of procedure for New Applications: timetables for information

respiratory syncytial virus vaccine - EMEA/H/C/006027 prevention of respiratory tract disease	**Accelerated review**
concizumab - EMEA/H/C/005938 routine prophylaxis to prevent or reduce the frequency of bleeding in patients with: haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors ≥ 12 years of age; haemophilia B (congenital factor IX deficiency) with FIX inhibitors of any age	
azacitidine - EMEA/H/C/006154 Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukaemia (CMML) and acute myeloid leukaemia (AML)	
exagamglogene autotemcel - EMEA/H/C/005763, ATMPtreatment of transfusion-dependent β-thalassemia and sickle cell disease	
pandemic influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/006052 Active immunisation for the prevention of disease caused by the influenza A virus H5N1 subtype contained in the vaccine	
elranatamab - EMEA/H/C/005908, Orphan Pfizer Europe MA EEIG, Treatment of adult patients with relapsed or refractory multiple myeloma	
cefepime / enmetazobactam - EMEA/H/C/005431 treatment of: 1) complicated urinary tract infections (including pyelonephritis); 2) hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP); 3) patients with bacteraemia that occurs in	

association with, or is suspected to be associated with, any of the infections listed above and 4) infections due to aerobic Gram-negative organisms in adults with limited treatment options
germanium (68ge) chloride / gallium (68ga) chloride - EMEA/H/C/006053 indicated for in vitro radiolabelling of specific carrier molecules to be used for positron emission tomography (PET) imaging
influenza virus a/turkey/turkey/1/2005 (h5n1) nibrg-23 strain, ha surface antigen - EMEA/H/C/006051 Prophylaxis of influenza
insulin human - EMEA/H/C/006011 treatment of patients with diabetes mellitus who require insulin for the maintenance of glucose homeostasis
omecamtiv mecarbil - EMEA/H/C/006112 treatment of adult patients with symptomatic chronic heart failure and reduced ejection fraction less than 30%
lecanemab - EMEA/H/C/005966 a disease modifying treatment in adult patients with Mild Cognitive Impairment due to Alzheimer’s disease and Mild Alzheimer’s disease (Early Alzheimer’s disease)
bevacizumab - EMEA/H/C/005723 Treatment of neovascular (wet) age-related macular degeneration (nAMD).
paclitaxel - EMEA/H/C/006173 treatment of metastatic breast cancer
nintedanib - EMEA/H/C/006179 treatment of non-small cell lung cancer (NSCLC)
paliperidone - EMEA/H/C/006185 Treatment of schizophrenia
omaveloxolone - EMEA/H/C/006084, Orphan Reata Ireland Limited, Treatment of Friedreich’s ataxia
pegcetacoplan - EMEA/H/C/005954 Treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

talquetamab - EMEA/H/C/005864, Orphan Janssen-Cilag International N.V., monotherapy treatment of adult patients with relapsed and refractory multiple myeloma	**Accelerated review**

B.6.2. Start of procedure for Extension application according to Annex I of Reg. 1234/2008): timetables for information

Azacitidine Accord - azacitidine - EMEA/H/C/005147/X/0013 Accord Healthcare S.L.U., Generic, Generic of Vidaza, Rapporteur: Hrefna Gudmundsdottir, PRAC Rapporteur: Menno van der Elst, "Extension application to introduce a new pharmaceutical form associated with a new strength (10 mg/ml powder for solution for infusion) and a new route of administration (intravenous use). The RMP version 2 is updated in accordance."	
Cufence - trientine - EMEA/H/C/004111/X/0014/G Univar Solutions BV, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Ana Sofia Diniz Martins, "Extension application to add a new strength (100 mg capsule, hard) grouped with a type IA variation (B.II.b.4.b) . The RMP (version 1.3) is updated in accordance. The marketing authorisation holder took the opportunity to align the PI to the latest QRD template (version 10.3)."	
Entyvio - vedolizumab - EMEA/H/C/002782/X/0075 Takeda Pharma A/S, Rapporteur: Armando Genazzani	
Kaftrio - ivacaftor / tezacaftor / elexacaftor - EMEA/H/C/005269/X/0033, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "Extension application to add a new pharmaceutical form (granules) associated with 2 new strengths (60 mg/40 mg/80 mg and 75 mg/50 mg/100 mg) to support a new indication in a combination regimen with ivacaftor for the treatment of cystic fibrosis (CF) in paediatric patients aged 2 to less than 6 years who have at least one F508del mutation in the CFTR gene (see section 5.1). The new indication is only applicable to the	

new granules pharmaceutical form. As a consequence of the line extension the PI for the film coated tablets is also updated to reflect the addition of a new pharmaceutical form. The RMP (version 6.2) has also been submitted."

Kalydeco - ivacaftor - EMEA/H/C/002494/X/0114/G

Vertex Pharmaceuticals (Ireland) Limited, Co-Rapporteur: Robert Porszasz, PRAC Rapporteur: Monica Martinez Redondo, "Extension application to add a new strength (59.5 mg) of the granules pharmaceutical form grouped with C.I.6.a, to support a new indication in a combination regimen with ivacaftor/tezacaftor/elexacaftor for the treatment of cystic fibrosis (CF) in paediatric patients aged 2 to less than 6 years who have at least one F508del mutation in the CFTR gene (see section 5.1). The RMP (version 15.1) has also been submitted.
Type IB B.II.f.1.b
The Product information has been updated accordingly."

Kalydeco - ivacaftor - EMEA/H/C/002494/X/0115/G

Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Robert Porszasz, PRAC Rapporteur: Monica Martinez Redondo, "Extension application to introduce a new strength (13.4 mg of ivacaftor granules in sachet), grouped with a type II variation (C.I.6.a) in order to extend the indication of the granule presentations to include children with cystic fibrosis aged 1 to less than 4 months of age and weighing 3 kg or more who have an R117H CFTR mutation or one of the approved 9 gating (class III) mutations based on interim results from study VX15-770-124 (study 124); this is a phase 3, 2-part, open-label study to evaluate the safety, pharmacokinetics, and pharmacodynamics of ivacaftor (IVA) in subjects with CF who are less than 24 months of age at treatment initiation and have a CFTR gating mutation. As a consequence, sections 1, 2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 6.3 and 8 of the SmPC of the granules presentations and sections 4.2, 4.8, 5.1 and 5.2 of the SmPC of the tablets presentations are updated. The

Labelling for the 13.4 mg granule presentation and the Package Leaflet of the granules and tablets presentations are updated in accordance. Version 15.2 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.
Type IA A.5.b
Type IA B.II.b.2.a"

PHEBURANE - sodium phenylbutyrate - EMEA/H/C/002500/X/0035
Eurocept International B.V., Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, "Extension application to introduce a new pharmaceutical form associated with a new strength (350 mg/ml oral solution).
The RMP (version 0.1) is updated in accordance."

Yuflyma - adalimumab - EMEA/H/C/005188/X/0022
Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to add a new strength (20 mg solution for injection). The indications for the new strength are identical to those already approved for the 40 mg strength. The RMP (version 2.1) has also been submitted. In addition, the MAH took the opportunity to include editorial changes ."

B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information

enalapril maleate ph. eur. - EMEA/H/C/005731, PUMA
treatment of heart failure
List of Questions adopted on 21.07.2022.

dabigatran etexilate - EMEA/H/C/005922
prevention of venous thromboembolic events
List of Questions adopted on 23.06.2022.

glofitamab - EMEA/H/C/005751, Orphan
Roche Registration GmbH, treatment of diffuse large B-cell lymphoma
List of Questions adopted on 15.09.2022.

pirtobrutinib - EMEA/H/C/005863, Orphan
Eli Lilly Nederland B.V., treatment of mantle cell lymphoma (MCL)

List of Questions adopted on 13.10.2022.

adagrasib - EMEA/H/C/006013
treatment of patients with advanced non-small cell lung cancer (NSCLC) with KRAS G12C mutation
List of Questions adopted on 15.09.2022.

lacosamide - EMEA/H/C/006047
treatment of epilepsy
List of Questions adopted on 15.09.2022.

futibatinib - EMEA/H/C/005627, Orphan
Taiho Pharma Netherlands B.V., treatment of cholangiocarcinoma
List of Questions adopted on 15.09.2022.

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/X/0078/G
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Armando Genazzani, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Rhea Fitzgerald, "Extension application to add a new strength of 75 mg of lumacaftor and 94 mg of ivacaftor fixed dose combination granules, grouped with a type II variation (C.I.6.a). C.I.6: Extension of indication to include treatment of cystic fibrosis for children aged 1 to less than 2 years 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 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."
List of Questions adopted on 13.10.2022.

eculizumab - EMEA/H/C/006036
treatment of paroxysmal nocturnal haemoglobinuria
List of Questions adopted on 10.11.2022.

sugammadex - EMEA/H/C/006046
reversal of neuromuscular blockade induced by rocuronium or vecuronium
List of Questions adopted on 15.09.2022.

Tenkasi - oritavancin - EMEA/H/C/003785/X/0036
Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski, "Extension

application to add a new strength of 1200 mg for powder for concentrate for solution for infusion. The RMP (version 4) is updated in accordance."
List of Questions adopted on 21.07.2022.

B.6.4. Annual Re-assessments: timetables for adoption

Defitelio - defibrotide -
EMEA/H/C/002393/S/0060, Orphan
Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Mari Thorn

Obizur - susoctocog alfa -
EMEA/H/C/002792/S/0050
Baxalta Innovations GmbH, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Brigitte Keller-Stanislawski

B.6.5. Renewals of Marketing Authorisations: timetables for adoption provided only if the validation has been completed

Defitelio - defibrotide -
EMEA/H/C/002393/R/0061, Orphan
Gentium S.r.l., Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Mari Thorn

Hulio - adalimumab -
EMEA/H/C/004429/R/0041
Viatris Limited, Rapporteur: Christophe Focke, Co-Rapporteur: Christian Gartner, PRAC Rapporteur: Ulla Wändel Liminga

Ilumetri - tildrakizumab -
EMEA/H/C/004514/R/0042
Almirall S.A, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Adam Przybylkowski

Kigabeq - vigabatrin -
EMEA/H/C/004534/R/0012
ORPHELIA Pharma SAS, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Kirsti Villikka

Koselugo - selumetinib -
EMEA/H/C/005244/R/0010, Orphan
AstraZeneca AB, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga

Lunsumio - mosunetuzumab -
EMEA/H/C/005680/R/0001, Orphan
Roche Registration GmbH, Rapporteur: Aaron

Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga

Mepsevii - vestronidase alfa - EMEA/H/C/004438/R/0033, Orphan
Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Maria del Pilar Rayon

Pelgraz - pegfilgrastim - EMEA/H/C/003961/R/0040
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Menno van der Elst

Slenyto - melatonin - EMEA/H/C/004425/R/0021
RAD Neurim Pharmaceuticals EEC SARL, Rapporteur: Kristina Dunder, Co-Rapporteur: Tomas Radimersky, PRAC Rapporteur: Ana Sofia Diniz Martins

Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/R/0038, Orphan
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Robert Porszasz, PRAC Rapporteur: Rhea Fitzgerald

Verzenios - abemaciclib - EMEA/H/C/004302/R/0025
Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Inês Ribeiro-Vaz

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

B.6.7. Type II Variations scope of the Variations: Extension of indication

Apexxnar - pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA/H/C/005451/II/0012
Pfizer Europe MA EEIG, Rapporteur: Daniela Philadelphy, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Jean-Michel Dogné, "Extension of indication to include infants, children and adolescents from 6 weeks to less than 18 years of age for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae,

based on final results from studies B7471003, B7471011, B7471012, B7471013 and B7471014. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted."

Bylvay - odevixibat - EMEA/H/C/004691/II/0011, Orphan

Albireo, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, "Extension of indication to include treatment of cholestasis and pruritus in Alagille syndrome (ALGS) in patients from birth and older for BYLVAY, based on final results from study A4250-012 and interim results from study A4250-015. Study A4250-012 is a 24-week, randomised, double-blind, placebo-controlled Phase III study conducted in 52 patients with a genetically confirmed diagnosis of ALGS and presence of pruritus and high serum bile acid levels at baseline. Study A4250-015 is an ongoing 72-week open-label extension trial for patients who completed study A4250-012 and evaluates the long-term safety and efficacy of Bylvay in patients with ALGS. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0027

Daiichi Sankyo Europe GmbH, Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Inês Ribeiro-Vaz, "Extension of indication to include the indication treatment of non-small cell lung cancer for Enhertu (trastuzumab deruxtecan), based on results from study DS8201-A-U204 (DESTINY-Lung01) and study DS8201-A-U206 (DESTINY-Lung02).
Study DESTINY-Lung01 is a phase 2, multicentre, open-label, 2-cohort study of trastuzumab deruxtecan (DS-8201a), an anti-HER2 antibody drug conjugate (ADC), for HER2-over-expressing or -mutated, unresectable

and/or metastatic non-small cell lung cancer (NSCLC) conducted at sites in Japan, the United States and Europe.
Study DESTINY-Lung02 is an ongoing phase 2, multicentre, randomised study to evaluate the safety and efficacy of trastuzumab deruxtecan in subjects with HER2-mutated metastatic non-small cell lung cancer, conducted in North America, Europe and Asia-Pacific.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
Version 2.2 of the RMP has also been submitted."

Foclivia - pandemic influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/001208/II/0081

Seqirus S.r.l, Rapporteur: Maria Grazia Evandri, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, "Extension of indication to include children from 6 months to less than 18 years of age for Foclivia, based on final results from study V87_30; this is a phase 2, randomized, observer-blind, multicentre study to evaluate the immunogenicity and safety of several doses of antigen and MF59 adjuvant content in a monovalent H5N1 pandemic influenza vaccine in healthy paediatric subjects 6 months to less than 9 years of age.
As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 4.9 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to bring it in line with the latest QRD template."

Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0052, Orphan

Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of indication to include the pre-treatment to reduce the risk of cytokine release syndrome (CRS) induced by glofitamab for Gazyvaro, based on results from study NP30179; this is a multicentre, open-label, Phase I/II study evaluating the safety, efficacy, tolerability and pharmacokinetics of escalating doses of glofitamab as a single agent and in

combination with obinutuzumab administered after a fixed, single dose pre-treatment of Gazyvaro in patients with relapsed/refractory B-cell NHL. As a consequence, sections 4.1, 4.2, 4.4, 5.1, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 10.0 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version."

Imfinzi - durvalumab - EMEA/H/C/004771/II/0057

AstraZeneca AB, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: David Olsen, "Extension of indication to include IMFINZI as treatment of adults with unresectable hepatocellular carcinoma (uHCC), based on final results from study D419CC00002 (HIMALAYA); this was a randomized, open-label, multi-centre phase III study of durvalumab and tremelimumab as first-line treatment in patients with unresectable hepatocellular carcinoma (HIMALAYA). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 9, Succession 1 of the RMP has also been submitted. In addition, the PI is brought in line with the latest QRD template version 10.3."

Jardiance - empagliflozin - EMEA/H/C/002677/II/0074

Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Maria del Pilar Rayon, "Extension of indication to include treatment of chronic kidney disease (CKD) for JARDIANCE, based on final results from study EMPA-KIDNEY (1245-0137) listed as a category 3 study in the RMP; this is a Phase III, multicentre international randomised parallel group double-blind placebo controlled clinical trial of empagliflozin once daily to assess cardio-renal outcomes in patients with chronic kidney disease. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 19.0 of the RMP has also been submitted. Furthermore, the PI is brought

in line with the latest QRD template version 10.3."

Olumiant - baricitinib - EMEA/H/C/004085/II/0037

Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, "Extension of indication to include the treatment of paediatric patients (from 2 years of age and older) with moderate to severe atopic dermatitis for OLUMIANT, based on the final results from study I4V-MC-JAIP; this is a Phase III, multicentre, randomised, double blind, placebo controlled, parallel-group, outpatient study evaluating the pharmacokinetics, efficacy, and safety of baricitinib in paediatric patients with moderate-to-severe atopic dermatitis. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet has been updated accordingly. Version 17.1 of the RMP has also been submitted."

Orencia - abatacept - EMEA/H/C/000701/II/0152

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Robert Porszasz, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to include the prophylaxis of acute Graft versus Host Disease (aGvHD) in the adult and paediatric population for Orencia, based on final results from studies IM101311 - Abatacept Combined With a Calcineurin Inhibitor and Methotrexate for Graft Versus Host Disease Prophylaxis and IM101841 - Overall Survival In 7/8 HLA-Matched Hematopoietic Stem Cell Transplantation Patients Treated With Abatacept Combined With A Calcineurin Inhibitor And Methotrexate - An Analysis Of The Centre For International Blood And Marrow Transplant Research (Cibmtr) Database. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 28.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Pepaxti - melphalan flufenamide - EMEA/H/C/005681/II/0002

Oncopeptides AB, Rapporteur: Paula Boudewina

van Hennik, Co-Rapporteur: Elita Poplavska, PRAC Rapporteur: Martin Huber, "Extension of indication to include treatment of patients with Multiple Myeloma who have received at least two prior lines of therapies for Pepaxti, based on final results from study OP-103 OCEAN; this is a randomized, open-label phase III study in patients with relapsed or refractory multiple myeloma following two to four lines of prior therapies and who were refractory to lenalidomide and the last line of therapy. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC."

Refixia - nonacog beta pegol - EMEA/H/C/004178/II/0032

Novo Nordisk A/S, Rapporteur: Daniela Philadelphy, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication to include treatment and prophylaxis of bleeding in children below 12 years of age with haemophilia B including previously untreated patients for Refixia, based on interim results from studies NN7999-3774 and NN7999-3895. NN7999-3774 is a multicentre, open-label, non-controlled study evaluating the safety, efficacy and pharmacokinetics of nonacog beta pegol in previously treated children with haemophilia B, while NN7999-3895 is a multicentre, open-label, single-arm, non-controlled trial evaluating the safety and efficacy of nonacog beta pegol in previously untreated patients with haemophilia B. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 5.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Retsevmo - selpercatinib - EMEA/H/C/005375/II/0021

Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst, "Extension of indication to include the treatment of adults and adolescents 12 years and older with advanced RET fusion-positive thyroid

cancer in the first-line setting for RETSEVMO based on interim data from studies LIBRETTO-001 (LOXO-RET-17001) and LIBRETTO-121; LIBRETTO-001 is an open-label, multicentre, global Phase 1/2 study of selpercatinib in patients with RET-altered advanced solid tumours. LIBRETTO-121 is a Phase 1/2 study of selpercatinib in paediatric patients with advanced RET-altered solid or primary central nervous system tumours. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.2 of the RMP has also been submitted."	
Retsevmo - selpercatinib - EMEA/H/C/005375/II/0022 Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, "Extension of indication for RETSEVMO to include the treatment of adults with advanced or metastatic RET fusion-positive solid tumours with disease progression on or after prior systemic therapies or who have no satisfactory therapeutic options, based on interim data from study LIBRETTO-001 (LOXO-RET-17001); LIBRETTO-001 is an open-label, multicentre, global Phase 1/2 study of selpercatinib in adult and adolescent patients with advanced RET-altered tumours. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC."	
TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0020 Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Extension of indication to include treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting, based on final results from study IMMU-132-09 (TROPiCS-02); this is an open-label, randomized, multicentre phase 3	

study of sacituzumab govitecan (IMMU-132) versus treatment of physician's choice (TPC) in subjects with hormonal receptor-positive (HR+) human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer (mBC) who have failed at least two prior chemotherapy regimens. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to update the list of local representatives in the Package Leaflet."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Voxzogo - vosoritide - EMEA/H/C/005475/II/0006, Orphan
BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Zane Neikena, "Extension of indication to include treatment of children less than 2 years of age for Voxzogo, based on final results from the category 1 study BMN 111-206 and interim results from its open-label extension study 111-208. 111-206 is a phase 2 randomized, double-blind, placebo-controlled, multicentre study to assess the safety and efficacy of BMN 111 in infants and young children with achondroplasia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

COMIRNATY - tozinameran - EMEA/H/C/005735/II/0165/G
BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson

COMIRNATY - tozinameran - EMEA/H/C/005735/II/0167
BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson

Cyramza - ramucirumab - EMEA/H/C/002829/II/0051

Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik

Dupixent - dupilumab - EMEA/H/C/004390/II/0069/G
Sanofi Winthrop Industrie, Rapporteur: Jan Mueller-Berghaus

ECALTA - anidulafungin - EMEA/H/C/000788/II/0052/G
Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege

Epidyolex - cannabidiol - EMEA/H/C/004675/II/0025/G, Orphan
GW Pharma (International) B.V., Rapporteur: Thalia Marie Estrup Blicher

EVUSHELD - tixagevimab / cilgavimab - EMEA/H/C/005788/II/0006/G
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus

EXPAREL liposomal - bupivacaine - EMEA/H/C/004586/II/0011/G
Pacira Ireland Limited, Rapporteur: Elita Poplavska

Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0143
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Idacio - adalimumab - EMEA/H/C/004475/II/0018/G
Fresenius Kabi Deutschland GmbH, Rapporteur: Johann Lodewijk Hillege

Nucala - mepolizumab - EMEA/H/C/003860/II/0057/G
GlaxoSmithKline Trading Services Limited, Rapporteur: Finbarr Leacy

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0195
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Sapropterin Dipharma - sapropterin - EMEA/H/C/005646/II/0010
Dipharma B.V., Generic, Generic of Kuvan, Rapporteur: Frantisek Drafi

Somavert - pegvisomant - EMEA/H/C/000409/II/0106/G
Pfizer Europe MA EEIG, Rapporteur: Jean-Michel

Race

Spikevax - elasomeran - EMEA/H/C/005791/II/0094/G
Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus

TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0119/G
Corza Medical GmbH, Rapporteur: Jan Mueller-Berghaus

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0115
MCM Vaccine B.V., Rapporteur: Christophe Focke

Vyvgart - efgartigimod alfa - EMEA/H/C/005849/II/0004/G, Orphan
Argenx, Rapporteur: Thalia Marie Estrup Blicher

WS2390
Januvia-EMEA/H/C/000722/WS2390/0080
Ristaben-EMEA/H/C/001234/WS2390/0074
Steglujan-EMEA/H/C/004313/WS2390/0019
TESAVEL-EMEA/H/C/000910/WS2390/0080
Xelevia-EMEA/H/C/000762/WS2390/0088
Merck Sharp & Dohme B.V., Lead Rapporteur: Kristina Dunder

WS2401/G
Hexacima-EMEA/H/C/002702/WS2401/0143/G
Hexyon-EMEA/H/C/002796/WS2401/0147/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects

Cibinqo - abrocitinib - EMEA/H/C/005452/II/0007
Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder, "To update section 5.1 of the SmPC in order to update long-term efficacy data based

on the results from studies B7451012, B7451013, B7451015 and B7451029."

EVOTAZ - atazanavir / cobicistat - EMEA/H/C/003904/II/0044

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, "Update of section 4.5 of the SmPC in order to update drug-drug interaction (DDI) information related to the co-administration with antiplatelet therapies classified as P2Y12 platelet inhibitors as well as the co-administration with dexamethasone and other corticosteroids. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0132

Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 4.8 of the SmPC in order to add optic neuritis to the list of adverse drug reactions (ADRs) with frequency rare based on literature review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes to the PI."

Lupkynis - voclosporin - EMEA/H/C/005256/II/0005

Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Kristina Dunder, "Update of sections 4.5 and 5.2 of the SmPC in order to update safety information based on final results from study AUR-VCS-2021-02 / Statin-DDI listed as REC in the Letter of Recommendation and study AUR-VCS-2016-02. AUR-VCS-2021-02 / Statin-DDI is an in-vivo DDI study, investigating the effects of voclosporin on simvastatin and its active metabolite simvastatin acid as substrates for OATP1B1/OATP1B3 and AUR-VCS-2016-02 was to show long-term (3 years) safety data from subjects receiving voclosporin and concomitant statins."

Methylthioninium chloride Proveblue - methylthioninium chloride - EMEA/H/C/002108/II/0054

Provepharm SAS, Rapporteur: Kristina Dunder, "Submission of the final report from studies PVP-2016003 and HQF-METHB-2018001. PVP-2016003 is an Open-label clinical study to

evaluate the safety and efficacy of ProvayBlue (methylene blue) for the treatment of acquired methemoglobinemia (MEBIPAM); while HQF-METHB-2018001 is a prospective, observational registry designed to collect real world data regarding the safety and efficacy of ProvayBlue."

Qutenza - capsaicin - EMEA/H/C/000909/II/0057

Grunenthal GmbH, Rapporteur: Bruno Sepodes, "Update of sections 4.4 and 4.8 of the SmPC in order to add `Third Degree Burn´ to the list of adverse drug reactions (ADRs) with frequency not known, based on a validated safety signal and post-marketing data; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to the Package Leaflet."

Reblozyl - luspatercept - EMEA/H/C/004444/II/0016, Orphan

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Daniela Philadelphy, "Update of section 5.1 of the SmPC in order to reflect the correct values of late-reported transfusions and modifications of previously reported transfusions based on final results from study ACE-536-B-THAL-001 (BELIEVE), A Phase 3, Double-Blind, Randomized, Placebo-Controlled, Multicentre Study To Determine The Efficacy And Safety Of Luspatercept (Ace-536) Versus Placebo In Adults Who Require Regular Red Blood Cell Transfusions Due To Beta-Thalassemia."

Retsevmo - selpercatinib - EMEA/H/C/005375/II/0023

Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce a new dose modification regimen in the event of 'interstitial lung disease (ILD)/pneumonitis' and to introduce it as a new warning and add it to the list of adverse drug reactions (ADRs) with frequency common, based on an internal safety review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor formatting changes to the PI."

Spikevax - elasomeran - EMEA/H/C/005791/II/0093

Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study QHD00028 (NCT04969276), a Phase II, open-label study to 'Assess the Safety and Immunogenicity of Fluzone High-Dose Quadrivalent (Influenza Vaccine), 2021-2022 Formulation and a Third Dose of Moderna COVID-19 Vaccine (mRNA-1273 Vaccine) Administered Either Concomitantly or Singly in Adults 65 Years of Age and Older Previously Vaccinated With a 2-dose Schedule of Moderna COVID-19 Vaccine'."

Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0048

Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study TMC114FD2HTX3002 (DIAMOND). This is a phase 3, single-arm, open-label study to evaluate the efficacy and safety of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) once daily fixed-dose combination (FDC) regimen in newly diagnosed, antiretroviral treatment-naïve human immunodeficiency virus type 1 (HIV-1) infected subjects receiving care in a test and treat model of care."

Tecovirimat SIGA - tecovirimat - EMEA/H/C/005248/II/0003/G

SIGA Technologies Netherlands B.V., Rapporteur: Jayne Crowe, "Grouped application consisting of the submission of the final reports from the following five non-clinical studies: 9603766 (SG2 material), 9603767 (SG2 Dimer material), 9603768 (SG1 material), 9603769 (SG1 exo-isomer material) and 9603770 (Maleic Anhydride material). These are genotoxicity studies for active drug substance impurities/degradants."

Ultomiris - ravulizumab - EMEA/H/C/004954/II/0034

Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study ALXN1210-PNH-302, a Phase III, randomised, open-label, active controlled study of ALXN1210 versus eculizumab in adult patients with

paroxysmal nocturnal hemoglobinuria (PNH) currently treated with eculizumab, listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly."

Veklury - remdesivir - EMEA/H/C/005622/II/0045

Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Update of section 5.1 of the SmPC in order to update clinical virology information based on results of the phenotypic analysis of the nsp12 substitutions that emerged post-treatment in study GS-US-540-5773, including T76I, A526V, A554V, E665K, and C697F."

Venclyxto - venetoclax - EMEA/H/C/004106/II/0045

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Submission of the final report from study M14-032 'A Phase 2 Open-Label Study of the Efficacy and Safety of Venetoclax ABT-199 (GDC-0199) in Chronic Lymphocytic Leukaemia Subjects with Relapse of Refractory to B-Cell Receptor Signaling Pathway Inhibitor Therapy' listed as a category 3 study in the RMP."

Xolair - omalizumab - EMEA/H/C/000606/II/0118

Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update long-term safety and efficacy based on results from XTEND study (ML29510), a Phase IV, multicentre, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of omalizumab through 48 weeks in patients with CSU."

WS2405
BYANNLI-
EMEA/H/C/005486/WS2405/0004
Trevicta-
EMEA/H/C/004066/WS2405/0030
Xeplion-
EMEA/H/C/002105/WS2405/0055

Janssen-Cilag International N.V., Lead Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC for Xeplion and Trevicta in order to modify the frequencies of the list of adverse drug reactions (ADRs) to align with the Product Information of BYANNLI. In addition,

the MAH took the opportunity to introduce administrative corrections and minor editorial changes to the PI as well as to update the list of local representatives in the Package Leaflet."

B.6.10. CHMP-PRAC assessed procedures

AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0042
Sanofi Winthrop Industrie, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Submission of the final report from study EFC11759 listed as a category 3 study in the RMP. This is a two-year, multicentre, randomized, double-blind, placebo-controlled, parallel group trial to evaluate efficacy, safety, tolerability and pharmacokinetics of teriflunomide administered orally once daily in paediatric patients with relapsing forms of multiple sclerosis (MS) followed by an open-label extension. The RMP version 8.0 has also been submitted."

AYVAKYT - avapritinib - EMEA/H/C/005208/II/0022, Orphan
Blueprint Medicines (Netherlands) B.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, "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 PI in line with the latest QRD template version 10.3."

GAVRETO - pralsetinib - EMEA/H/C/005413/II/0010
Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga, "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 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."

Lumykras - sotorasib - EMEA/H/C/005522/II/0007

Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Marie Louise Schougaard Christiansen, "Update of sections 4.2 and 5.2 of the SmPC in order to update recommendations for patients with moderate to severe hepatic impairment following final results from study 20200362 listed as a category 3 PASS study in the EU RMP; this is a Phase I clinical study to evaluate the pharmacokinetics (PK) of a single oral dose of sotorasib administered in subjects with moderate or severe hepatic impairment compared with subjects who have normal hepatic function. The EU RMP version 1.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.3."

MINJUVI - tafasitamab - EMEA/H/C/005436/II/0008, Orphan

Incyte Biosciences Distribution B.V., Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.4 of the SmPC in order to add a new warning on Progressive Multifocal Leukoencephalopathy (PML) based on post-marketing data; the Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and to bring the PI in line with the latest QRD template version 10.3."

Piqray - alpelisib - EMEA/H/C/004804/II/0018

Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.5 and 5.2 of the SmPC in order to update drug-drug interaction information, based on final results from study BYL719A2111; this is a phase 1, open-label,

fixed-sequence, two-period drug-drug interaction (DDI) study evaluating the PK probe substrates for CYP3A4, CYP2B6, CYP2C8, CYP2C9, and CYP2C19 when administered either alone or in combination with repeated doses of alpelisib. The Annex II and Package Leaflet are updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Polivy - polatuzumab vedotin - EMEA/H/C/004870/II/0020, Orphan

Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga, "To submit the updated final OS CSR for study GO39942 - A Phase III, multicentre, randomized, double-blind, placebo-controlled trial comparing the efficacy and safety of polatuzumab vedotin in combination with R-CHP versus R-CHOPin previously untreated patients with DLBCL (POLARIX) listed as a category 3 study in the RMP. This submission will address the missing information of "long-term safety" in patients treated with polatuzumab vedotin.
An updated RMP version 4.0 has also been submitted to remove the commitment for this study along with the missing information of "long-term safety"."

TUKYSA - tucatinib - EMEA/H/C/005263/II/0010

Seagen B.V., Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Jean-Michel Dogné, "Submission of the final report from study SGNTUC-017 (MOUNTAINEER) listed as a category 3 study in the RMP. This is a Phase 2, Open Label Study of Tucatinib Combined with Trastuzumab in Patients with HER2+ Metastatic Colorectal Cancer. Primary objective is to determine the antitumor activity of tucatinib given in combination with trastuzumab. The RMP version 1.1 has also been submitted."

Vabysmo - faricimab - EMEA/H/C/005642/II/0002

Roche Registration GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Inês Ribeiro-Vaz, "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, randomized, 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 PI."

Veklury - remdesivir - EMEA/H/C/005622/II/0044/G

Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová, "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 randomized, double-blind, placebo-controlled, parallel group, multicentre study evaluating the efficacy and safety of remdesivir in participants with severely reduced kidney function who were hospitalised for COVID-19, while study GS-US-540-9015 is a phase 1, multicentre, open-label, single-dose study to evaluate the single-dose 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 PI."

Veklury - remdesivir - EMEA/H/C/005622/II/0046

Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová, "Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy and breast-feeding based on final results from study IMPAACT 2032 listed as a category 3 study in the RMP; this is a phase 4, prospective, open-label, non-randomized study to address PK and safety of remdesivir in pregnant women. The

Package Leaflet is updated accordingly. The RMP version 5.2 has also been submitted."

B.6.11. PRAC assessed procedures

PRAC Led

Brukinsa - zanubrutinib - EMEA/H/C/004978/II/0008

BeiGene Ireland Ltd, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Paula Boudewina van Hennik, "Submission of the updated RMP (Version 3.0) on the dates of submission of information to the ongoing study BGB-3111-LTE1."

PRAC Led

Coagadex - human coagulation factor x - EMEA/H/C/003855/II/0046, Orphan

BPL Bioproducts Laboratory GmbH, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study TEN06 - NCT03161626 (REC EMEA/H/C/003855). This is a non-interventional, multicentre, post-marketing registry study in three patients with moderate or severe hereditary FX deficiency, to assess Coagadex administered peri-operatively for haemostatic cover in major surgery during routine post-marketing use. The primary objective is to collect additional surgical data on the clinical effectiveness of Coagadex, in a post-marketing environment, for peri-operative haemostatic cover during major surgery in patients with moderate or severe hereditary factor X (FX) deficiency. The RMP version 3.0 has also been submitted."

PRAC Led

Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0093

Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final non-interventional Pompe Registry Report 2022 (MEA024 and MEA025)."

PRAC Led

Ocaliva - obeticholic acid - EMEA/H/C/004093/II/0039, Orphan

Advanz Pharma Limited, PRAC Rapporteur:

Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 2.0 in order to change to EU Qualified Person for Pharmacovigilance (QPPV), update the list of safety concerns and study data for 747-302 and 747-401."

PRAC Led

OPDIVO - nivolumab -
EMEA/H/C/003985/II/0127

Bristol-Myers Squibb Pharma EEIG, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from the post-authorisation safety study (PASS) CA209835: A registry study in patients who underwent post-nivolumab allogeneic haematopoietic stem-cell transplantation (HSCT). This study is listed as a category 3 study in the RMP. An updated RMP version 31.0 has also been submitted."

PRAC Led

Ozurdex - dexamethasone -
EMEA/H/C/001140/II/0044

AbbVie Deutschland GmbH & Co. KG, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated Annex II and RMP version 11 in order to remove additional risk minimisation measure: Patient guide, audio CD (where required)."

PRAC Led

Parsabiv - etelcalcetide -
EMEA/H/C/003995/II/0021

Amgen Europe B.V., PRAC Rapporteur: Valentina Di Giovanni, PRAC-CHMP liaison: Armando Genazzani, "Submission of the final report from study 20170561 listed as a category 3 study in the RMP. This is an observational PASS to evaluate the potential association between Parsabiv and gastrointestinal bleeding."

PRAC Led

Simponi - golimumab -
EMEA/H/C/000992/II/0111

Janssen Biologics B.V., PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of section 4.6 of the SmPC in order to update information on pregnancy based on final results from PASS study

CNTO148ART4001 listed as a category 3 study in the RMP; this is an observational prospective cohort study to collect and analyse information pertaining to pregnancy outcomes of women exposed to golimumab during pregnancy. The RMP version 23.2 has also been submitted."

PRAC Led

Simponi - golimumab - EMEA/H/C/000992/II/0112

Janssen Biologics B.V., PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study P04480 (RABBIT) listed as a category 3 study in the RMP. This is an observational prospective cohort study to evaluate the long-term safety of treatment with biologics in rheumatoid arthritis. The RMP version 23.3 has also been submitted."

PRAC Led

Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0039, Orphan

Vertex Pharmaceuticals (Ireland) Limited, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of the final report from PASS study VX17-661-117 listed as a category 3 study in the RMP. This is an Observational Study to Evaluate the Utilization Patterns and Real-World Effects of Tezacaftor and Ivacaftor Combination Therapy (TEZ/IVA) in Patients With Cystic Fibrosis (CF). The RMP version 3.4 has also been submitted."

PRAC Led

Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0040, Orphan

BioMarin International Limited, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP version 6.0 in order to correct the objectives of MARS in the RMP to be consistent with version 6 of the protocol and to update the "Method used to calculate exposure" due to GDPR restrictions following the assessment of procedures PSA/S/0062 and PSUSA/00010218/202102."

PRAC Led

XOSPATA - gilteritinib - EMEA/H/C/004752/II/0012, Orphan

Astellas Pharma Europe B.V., PRAC Rapporteur:

Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of the final report from study 2215-PV-0001 - Evaluation of the effectiveness of the Xospata Routine Risk Minimisation Measures (RMMs) and an additional Risk Minimisation Measure (aRMM): A Cross sectional study among Healthcare Professionals to assess awareness and knowledge, listed as a category 3 study in the RMP. The RMP version 3.0 has also been submitted."

PRAC Led

Zavesca - miglustat -
EMEA/H/C/000435/II/0076

Janssen-Cilag International N.V., PRAC Rapporteur: Mari Thorn, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 15.1 in order to remove risks in line with GVP module V revision 2. The MAH has also taken the opportunity to introduce minor changes, such as update of the post-marketing exposure data and alignment with the latest Company EU-RMP Template."

PRAC Led

WS2402
Advagraf-
EMEA/H/C/000712/WS2402/0069
Modigraf-
EMEA/H/C/000954/WS2402/0045

Astellas Pharma Europe B.V., Lead PRAC Rapporteur: Ronan Grimes, PRAC-CHMP liaison: Jayne Crowe, "C.I.11.z - To update the EU Risk Management Plan with the new TPRI final study submission milestone, related to procedure EMEA/H/C/000712/MEA030 and EMEA/H/C/000954/MEA022 (study F506-PV-0001)."

PRAC Led

WS2430
Exviera-EMEA/H/C/003837/WS2430/0056
Viekirax-
EMEA/H/C/003839/WS2430/0068

AbbVie Deutschland GmbH & Co. KG, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "C.I.11.z - To update the RMP for Viekirax and Exviera to include the completion of studies B16-959, B20-146, M14-423 (TOPAZ-I) and M14-222 (TOPAZ-II), following the outcome of EMEA/H/C/PSR/J/0038, EMEA/H/C/WS2216 and

EMEA/H/C/WS2304, respectively. The MAH proposes to remove the emergence and recurrence of hepatocellular carcinoma as potential risks and update the related pharmacovigilance activities and other sections of the RMPs."

PRAC Led
WS2434
Entresto-
EMEA/H/C/004062/WS2434/0049
Neparvis-
EMEA/H/C/004343/WS2434/0047
Novartis Europharm Limited, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "C.I.11.z - To amend the RMP for Ernestro and its duplicate marketing authorisation Neparvis to update the milestones for MEA 002 (study CLCZ696B2014) and MEA 004 (study CLCZ696B2015) ."

PRAC Led
WS2435
Entresto-
EMEA/H/C/004062/WS2435/0048
Neparvis-
EMEA/H/C/004343/WS2435/0046
Novartis Europharm Limited, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of the final report from study CLCZ696B2013 listed as a category 3 study in the RMP. Study CLCZ696B2013 is a non-interventional, post-authorization, database cohort study to assess the risk of serious angioedema in association with LCZ696 (sacubitril/valsartan; Entresto) use in Black patients with heart failure in the United States."

B.6.12. CHMP-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0022/G, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0013/G, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Concetta Quintarelli, CHMP Coordinator:

Armando Genazzani

WS2389/G
Tecartus-
EMEA/H/C/005102/WS2389/0031/G
Yescarta-
EMEA/H/C/004480/WS2389/0059/G
Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

B.6.15. Unclassified procedures and worksharing procedures of type I variations

WS2410
Glyxambi-
EMEA/H/C/003833/WS2410/0050
Jardiance-
EMEA/H/C/002677/WS2410/0077
Synjardy-
EMEA/H/C/003770/WS2410/0069
Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS2411/G
Copalia HCT-
EMEA/H/C/001159/WS2411/0104/G
Dafiro HCT-
EMEA/H/C/001160/WS2411/0106/G
Exforge HCT-
EMEA/H/C/001068/WS2411/0103/G
Novartis Europharm Limited, Lead Rapporteur: Thalia Marie Estrup Blicher

WS2413/G
Axura-
EMEA/H/C/000378/WS2413/0083/G
Memantine Merz-
EMEA/H/C/002711/WS2413/0019/G
Merz Pharmaceuticals GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro

WS2417/G
Ongentys-
EMEA/H/C/002790/WS2417/0055/G
Ontilyv-
EMEA/H/C/005782/WS2417/0010/G
Bial - Portela & Cª, S.A., Lead Rapporteur:

Martina Weise

WS2420
Nuwiq-EMEA/H/C/002813/WS2420/0052
Vihuma-
EMEA/H/C/004459/WS2420/0034
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY

B.7.1. Yearly Line listing for Type I and II variations

B.7.2. Monthly Line listing for Type I variations

B.7.3. Opinion on Marketing Authorisation transfer (MMD only)

B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)

B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)

B.7.6. Notifications of Type I Variations (MMD only)

C. Annex C - Post-Authorisation Measures (PAMs), (Line listing of Post authorisation measures with a description of the PAM. Procedures starting in that given month with assessment timetabled)

D. Annex D - Post-Authorisation Measures (PAMs), (Details on PAMs including description and conclusion, for adoption by CHMP in that given month, or finalised ones with PRAC recommendation and no adoption by CHMP needed)

E. Annex E - EMA CERTIFICATION OF PLASMA MASTER FILES

Information related to plasma master files cannot be released at the present time as these contain commercially confidential information.

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

E.2. Time Tables – starting & ongoing procedures: For information

PMF timetables starting and ongoing procedures	Tabled in MMD and sent by post mail (folder E).

F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver

G. ANNEX G

G.1. Final Scientific Advice (Reports and Scientific Advice letters):

Information related to Scientific Advice cannot be released at the present time as these contain commercially confidential information.

G.2. PRIME

Some information related to PRIME cannot be released at the present time as these contain commercially confidential information.

G.2.1. List of procedures concluding at 23-26 January 2023 CHMP plenary:

Oncology	
Treatment of prostate cancer (SME)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Indicated for patients with locally advanced squamous cell carcinoma of the head and neck	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Treatment of non-muscle invasive bladder cancer	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Treatment of patients with stage IIIB or stage IV non-small cell lung cancer (NSCLC) not amenable to EGFR/ALK/ROS based therapy, who are treatment-naïve for advanced/metastatic disease (1st line NSCLC) (SME)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Cardiovascular diseases	
ApTOLLTreatment of Acute Ischemic Stroke (SME)	The CHMP granted eligibility to PRIME and adopted the critical summary report.
Other - Congenital, familial and genetic disorders	

GNT0003 Treatment of severe Crigler-Najjar syndrome in adults and children >10 years old, requiring phototherapy ATMP	The CAT and CHMP granted eligibility to PRIME and adopted the critical summary report.

G.2.2. List of procedures starting in January 2023 for February 2023 CHMP adoption of outcomes

H. ANNEX H - Product Shared Mailboxes – e-mail address